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Short communication

Image analysis of surface colour of film-coated tablets

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Introduction

The appearance of the dosage form (qualitative description of the shape and colour) is the first parameter of the specification for quality testing performed to confirm that the products are acceptable for their intended use. Any change of these characteristics during manufacture or storage indicate on the quality issues and require further, investigation (including quantitative methods) and taking appropriate actions (ICH Harmonised Tripartite Guideline Q6A, 1999). The surface colour of film-coated tablets has a significant importance in quality control as well as recognition and is an important factor that contributes to the detection of falsified medicines (Laksmana et al., 2009; do Prado Pugliaa et al., 2021; Rodomonte et al., 2010). However, sometimes it is quite difficult and challenging to visually detect changes in the colour of film-coated tablets and there is a need for more sophisticated method (colorimetric method or image analysis using an appropriate software) (Farkas et al., 2021).

The image analysis is based on the use of a stereomicroscope and image processing software allowing to highlight the differences which cannot be detected visually. The testing procedure has to be performed under specified conditions (illumination and focus) with high precision because even slight changes in the camera's lenses, sensor or the light could impact the results significantly (Rebiere et al., 2014).

The aim of this study was to develop standardized method for image analysis of different film-coated tablets, containing same active ingredient and same colour of the film-coating, produced by different manufacturers.

Materials and methods

Materials

For this research three types of film coated tablets (each considered as tablet sample) containing 100 mg/tablet sildenafil as active substance, from a different manufacturers, with the declared same composition of the colouring excipients in the film-coating.

Stemi 508 stereomicroscope (Carl Zeiss Microscopy GmbH, Germany) was used, equipped with a built-in Axiocam ERc 5s (0.5x). Image analysis was performed using Zeiss ZEN 2.6 (Blue edition) software. Statistical analysis was performed using Microsoft excel 2013 edition.

Method

Each side of the tablets was photographed under a steromicroscope with the built-in camera. Same position of the tablet and same settings in illumination and focus (zoom 0.3x) were used for each acquisition. The tablets were manually centred against a white background, and the images were captured using light in the visible region with automatically adjustment of the exposure. Standard method for live image settings: contrast (black value 0), brightness (white value 255) and gamma value of 0.45, were used for all images. The saved images where further evaluated using the Zeiss ZEN 2.6 (Blue edition) software. The obtained results were extracted in Excel files and analysed statistically using Schewart diagrams.

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Results and discussion

Visually all tested tablet samples appeared with the blue colour, with various size and shape. The difference in the shade of the colour could be identified visually only in the one tablet sample.

Image analysis included comparison of the colour distribution plots obtained using image processing tools provided in Zeiss ZEN 2.6 (Blue edition) software. The optimum colour presentation was used for capturing the images by adjusting the values for Contrast (Black value 0), Gamma value (0.45) and Brightness (White value 255) in the live image settings. In order to ensure reproducible results, the settings for image capture and image processing were saved as a standard method and used for all tested samples.

The scatter plot displaying the pixel distribution for each image, and data table were correlated for each tablet within each tablet sample. 3D visualization of the images provided comparison of the density structure of the surface colour of the tablets. Three regions from each image were selected for evaluation of the colour distribution: upper left and right region, as well as the middle part of the tablet, taking into consideration not to include the engraved letters. Data with measured values for both: the entire image and the individual regions were exported as excel files and analysed statistically.

The data tables provided by the software included individual values of the colour distribution for the red, green and blue colour, with descriptive statistic parameters. The average values for each colour (red, green and blue) obtained from images of tablets within each sample, were plotted on Shewart X-bar chart. Average value of all points was used as central line. The control limits were based on variation between the groups of measurements and calculated as: Central line ± 3 × SD. The distribution of the values within each chart was within the upper and lower control limit, indicating that the applied method can be used for control of the variations of the colour of the tablet film-coating due to variations in manufacturing process and issues with stability. Implementation of reproducible and robust manufacturing process will provide distribution of the colour within the defined control limits.

The scatter plot displaying the pixel distribution values and the 3D image of the data of the colour distribution for the tablets, from different manufacturers were compared. The results have shown that the applied method of image analysis is able to detect the differences between the colours of the film-coated tablets produced by different manufactures.

Further studies are needed to expand the testing on a large sample size and to include the batch to batch variability.

Conclusion

Standardized method for characterization of the colour of film-coated tablets, based on image analysis was developed. With the proposed method it is possible to identify the differences between the colours of the film-coated tablet containing same active ingredient with the same strength, and the same composition of the colouring excipients in the film-coating, produced by different manufacturers.

Image analysis is a non-destructive method, which can be used as a fast and effective analytical tool for characterization of the colour of film coated tablets, as well as for other pharmaceutical dosage forms. Additionally, it enables effective monitoring of possible differences and changes in the manufacturing process or storage of the pharmaceutical dosage form, as well as an initial tool for identification of falsified pharmaceutical products.

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