A Concise Quality Control Guide On Essential Drugs And Other Medicines

Manual

Accompanying The GPHF-Minilab®

Extension 2002
Ten New Drugs
Plus Chloroquine

Second Supplement To Volume I
Colour Reactions

GPHF
German Pharma Health Fund e.V.

An Initiative of Research Based Pharmaceutical Companies in Germany

Contents

7.21 Artesunate (Artemether, Dihydroartemisinin)

Primary Screening via Visual Inspection & Disintegration Test

I. VISUAL INSPECTION

Search for deficiencies on labelling, packaging and dosage forms as described in the opening chapters on general methods and operations of the main manual. Write down all product particulars using the *Reporting Form* as a guide. Each tablet or capsule usually contains 50 or 200 mg of artesunate.

II. DISINTEGRATION TEST

All quick release artesunate tablets and capsules must pass the disintegration test as described in the opening chapters on general methods and operations of the main manual. They should disintegrate in water at 37 °C in less than 30 minutes. It is a major defect if a drug product does not pass this test.

III. RESULTS & ACTIONS TO BE TAKEN

Drug products from unusually cheap sources, drug products with missing or incorrect accompanying documents and drug products with defective dosage forms, packaging or with incomplete, damaged or missing labels or with labels written in a foreign language should be subjected to both, a colour identity test and thin-layer chromatographic assay.

Verification of Identity via Colour Reaction

I. EQUIPMENT AND REAGENTS

1) Circular filter paper
2) Pestle
3) Microspoon
4) Graduated test-tube
5) pH indicator test paper
6) Water
7) Sodium hydroxide test solution 8%
8) Glacial acetic acid
9) Fast Red TR Salt test solution with a dye content of about 0.2%

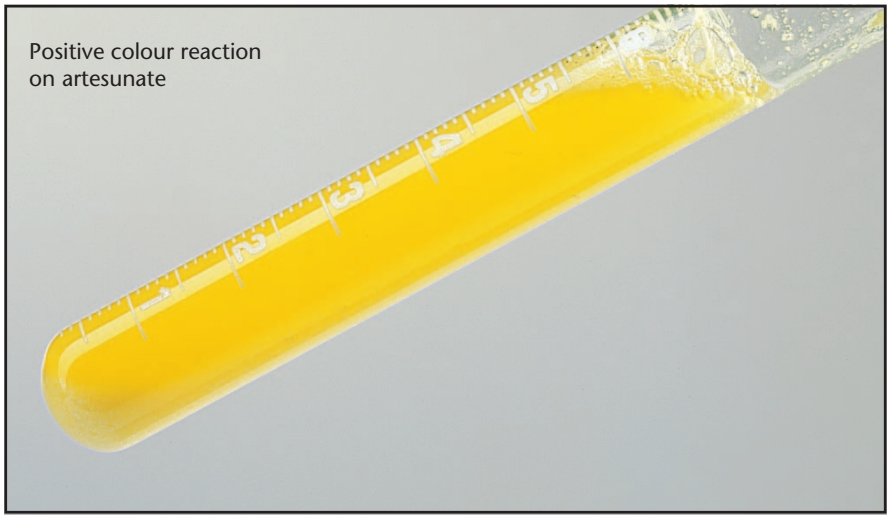
II. SAMPLE PREPARATION

Put one tablet on a circular filter paper. Break down the tablet into small bits and pieces using a pestle. Grind till a fine powder is produced.
Seperate the coating from the powder if a colour-coated tablet has been used. If the drug has been formulated as a capsule just open one by carefully separating the cap from the bottom shell and use the powder content directly.
Place 5 to 10 microspoons of the powder obtained into the test-tube. This will be your sample.

III. COLOUR REACTION

Add to the sample 2.5 ml of *water* followed by 2.5 ml of *sodium hydroxide solution 8%*, shake thoroughly, and allow the solution to sit for 15 minutes at room temperature. Now, add 30 drops of *glacial acetic acid*, thoroughly shake the test-tube again and confirm that the solution has been properly acidified using the pH indicator test paper supplied. Finally, add 0.5 ml of *Fast Red TR solution 0.2%* and shake again; a vivid lemon colour is instantly produced.
Repeat the examination with two other samples thus eliminating anomalous results. Perform also blank runs.

IV. COLOUR OBSERVED



Positive colour reaction on artesunate

V. RESULTS & ACTIONS TO BE TAKEN

Confirm the drug's identity and verify its potency via a thin layer chromatographic assay if the product shows a positive respond on the colour reaction performed. Do not spoil valuable resources from the TLC kit on batches definitely failing to produce the colour requested. In this case, reject the batch and retain some samples. Refer to a fully equipped drug quality control laboratory for further investigation. Put the batch on quarantine till a final decision on rejection or release has been taken.

VI. OUTLOOK: ARTEMETHER & DIHYDROARTEMISININ

Fast Red TR salt reacts with an alkali induced decomposition product of artesunate to form the distinct yellow colour shown above after the solution has been acidified with glacial acetic acid. However, that assay is specific for artesunate only. Because of concerns over potential artemether tablet counterfeiting, the colour reaction on artesunate was later modified by M. D. Green (Centers for Disease Control and Prevention in Atlanta, USA) to detect also artemether and dihydroartemisinin in solid dosage forms. Detailed modification procedures are given in "Authentication of Artemether, Artesunate, and Dihydroartemisinin Antimalarial Tablets Using a Simple Calorimetric Method", *Tropical Medicine and International Health, 6(12):980-982, 2001.*

The assay procedure described there is as follows: Scrape about 5% of the tablet mass into a glass tube, add 0.4 ml of methanol and mix for about 10 seconds. Add 0.4 ml of 5 N HCl and incubate the sample at room temperature (22 - 27 °C) for at least one hour. Add 2.2 ml of buffering solution consisting of 0.1 M borate in 5% ammonia solution. Add 0.1 ml of Fast Red TR salt solution (5 or 10 mg/ml water) and thoroughly mix. A yellow colour develops within 5 minutes if artemether, dihydroartemisinin or artesunate is present in the sample. There is a patent pending on this method.