A Concise Quality Control Guide on Essential Drugs and other Medicines

Manual

Accompanying the GPHF-Minilab™

Supplement 2026 on ibuprofen

Physical Testing & Thin-Layer Chromatography

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7.126 Ibuprofen

Primary Screening on Product Deficiencies by Physical Testing

I. PHYSICAL TESTING

During 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 and report the findings. Consider to take pictures, for example, with a smartphone camera. Each tablet usually contains 200, 400 or 600 mg of ibuprofen per free base. Other dosage strengths are known to exist. Verify the total weight of tablets and capsules using the electronic pocket balance provided. All quick release ibuprofen tablet and capsule formulations have to pass the disintegration test as described at the beginning of the main manual. They should disintegrate in water at 37 °C in less than 30 minutes. It is a major defect if an instant release formulation does not pass this test.

II. RESULTS & ACTIONS TO BE TAKEN

Medicinal products from unusually cheap sources, medicinal products with missing or incorrect accompanying documents and medicinal products with defective dosage forms, packaging or with incomplete, damaged or missing labels or with labels in a foreign language or medicinal products held under poor storage conditions should be subjected to a thin-layer chromatographic test.

Verification of Drug Identity and Content by Thin-Layer Chromatography

I. PRINCIPLE

Ibuprofen is extracted from tablets or capsules with a known volume of methanol and is subsequently checked for identity and content by thin-layer chromatography (TLC) in comparison with a suitable secondary standard.

II. EQUIPMENT AND REAGENTS

1) Pestle
2) Aluminium foil
3) Funnel
4) Spatula
5) Label tape
6) Marker pen
7) Pencil and ruler
8) 10-ml vials
9) Set of graduated pipettes (1 to 25 ml)
10) Set of laboratory glass bottles (25 to 100 ml)
11) TLC aluminium plates pre-coated with silica gel 60 F_{254}, size 5x10 cm
12) Glass microcapillaries (2-µl filling capacity)
13) TLC developing chamber (500-ml jar)
14) Hot plate
15) Filter paper
16) Pair of scissors
17) Pair of tweezers
18) Electronic pocket balance
19) UV light of 254 nm
20) Plastic beaker (250 ml)
21) Potassium permanganate
22) Sodium carbonate (anhydrous)
23) Sodium hydroxide (granulated)
24) Toluene
25) Acetone
26) Methanol
27) Ammonia solution 25%
28) Distilled/tap/bottled water
29) Reference agent, for example, ibuprofen 200 mg tablets

III. PREPARATION OF THE STOCK STANDARD SOLUTION

The preparation of the stock standard solution requires an authentic medicinal product for reference purposes, for example, tablets containing 200 mg of ibuprofen. Wrap up one reference tablet into aluminium foil and crush it down to a fine powder using a pestle. Carefully empty the aluminium foil over a 25-ml laboratory glass bottle and wash down all residual solids with 10 ml of methanol using a graduated pipette. Close the lab bottle and shake for about three minutes until most of the solids are dissolved. Allow the solution to stand for an additional five minutes until undissolved

residues settle below the supernatant liquid. The solution obtained should contain 20 mg of total ibuprofen per ml and be labelled as *'Ibuprofen Stock Standard Solution'*. Freshly prepare this solution for each test. Continue to work with the clear or hazy supernatant liquid.

IV. PREPARATION OF THE WORKING STANDARD SOLUTION 100% (UPPER WORKING LIMIT)

Pipette 1 ml of the stock standard solution into a 10-ml vial and add 3 ml of methanol. Close and shake the vial. The solution obtained should contain 5 mg of total drug per ml and be labelled as *'Ibuprofen Working Standard Solution 100%'*.

This higher working standard solution represents a drug product of good quality containing 100 % of ibuprofen.

V. PREPARATION OF THE WORKING STANDARD SOLUTION 80% (LOWER WORKING LIMIT)

Pipette 1 ml of the stock standard solution into a 10-ml vial and add 4 ml of methanol using suitable graduated pipettes. Close and shake the vial. The solution obtained should contain 4 mg of total ibuprofen per ml and be labelled as *'Ibuprofen Working Standard Solution 80%'*.

This lower working standard solution represents a medicinal product of poor quality containing just 80% of the amount of ibuprofen as stated on the product's label. In the current investigation, this level of ibuprofen represents the lower acceptable limit for a given product. Pharmacopoeial limits do not apply in our context.

VI. PREPARATION OF THE STOCK SAMPLE SOLUTION FROM A PRODUCT CLAIMING TO CONTAIN 200 MG OF IBUPROFEN PER UNIT

Take a whole tablet or capsule from a suitable medicinal product sampled in the field. As usual, tablets are wrapped up into aluminium foil and crushed down to a fine powder using a pestle. Transfer all the powder obtained into a 25-ml laboratory glass bottle. Powder obtained from sample capsules should be placed directly in the bottle adding the empty cap and body shells last. For extraction, add 10 ml of methanol using a suitable graduated pipette. Then, close the bottle and shake for about three minutes until most of the solids are dissolved. Allow the solution to stand for an additional five minutes until undissolved residues settle below the supernatant liquid.

400 MG OF IBUPROFEN PER UNIT

Place the powder obtained from a whole sample tablet or capsule into a 25-ml laboratory glass bottle, add 20 ml of methanol with a suitable graduated pipette and extract the ibuprofen. Continue working as described above.

600 MG OF IBUPROFEN PER UNIT

Place the powder obtained from a whole sample tablet or capsule into a 50-ml laboratory glass bottle, add 30 ml of methanol with a suitable graduated pipette and extract the ibuprofen. Continue working as described above.

800 MG OF IBUPROFEN PER UNIT

Place the powder obtained from a whole sample tablet or capsule into a 50-ml laboratory glass bottle, add 40 ml of methanol with a suitable graduated pipette and extract the ibuprofen. Continue working as described above.

All stock sample solutions produced should finally contain 20 mg of total ibuprofen per ml and be labelled as *'Ibuprofen Stock Sample Solution'*. Freshly prepare these solutions for each test. Continue working with the clear or hazy supernatant liquids.

VII. PREPARATION OF THE WORKING SAMPLE SOLUTION

Pipette 1 ml of the stock sample solution into a 10-ml vial and add 3 ml of methanol. Close and shake the vial and label as *'Ibuprofen Working Sample Solution'*.

The expected concentration of ibuprofen in this working sample solution is 5 mg per ml and should match the concentration of ibuprofen of the higher working standard solution produced above.

VIII. SPOTTING

Mark an origin line parallel to and about 1.5 cm from the bottom edge of the chromatoplate and apply 2 µl of each test and standard solution as shown in the picture at the end of this protocol using the microcapillary pipettes supplied.

Up to five spots can be placed on a plate. Check the uniformity of all spots using UV light of 254 nm. All spots should be circular in shape and equally spaced across the origin line. Although their intensities might differ, their diameters never should. Different intensities are due to residual amounts of excipients or different drug concentrations in the sample solutions. A difference in spot size, however, relates to poor spotting. Repeat this step if homogeneous spotting is not achieved first time.

Gently dry the spots. To do this, hold the chromatoplate with the supplied tweezers in the hot air stream directly above the heating plate for about 15 seconds. Shake the TLC plate constantly and each time the chromatoplate moves downwards, its underside is allowed to touch the surface of the heating plate for fractions of a second.

IX. DEVELOPMENT

Using suitable graduated pipettes and a transfer pipette, add 17 ml of acetone, 1 ml of toluene, 1.9 ml of water and 2 drops of ammonia solution 25% to a clean and dry jar serving as TLC developing chamber. Close the chamber and mix thoroughly. Line the chamber's wall with filter paper and wait for about 15 minutes thus ensuring saturation of the chamber with solvent vapour at ambient temperature. When the loaded TLC plate is placed in the chamber, it should be placed in as quickly as possible to ensure a limited loss of chamber saturation whilst the lid is off. Close the jar and develop the chromatoplate until the solvent front has moved about three-quarters of the length of the plate, the developing time being about 12 minutes. Remove the TLC plate from the chamber, mark the solvent front and allow excess solvent to evaporate by gentle drying. To do this, hold the chromatoplate with the supplied tweezers in the hot air stream directly above the heating plate for about one minute. Shake the TLC plate constantly and each time the chromatoplate moves downwards, its underside is allowed to touch the surface of the heating plate for fractions of a second.

X. DETECTION

Stain the developed chromatography plate with a potassium permanganate solution. Prepare the staining solution by dissolving 125 mg of sodium hydroxide, 3.7 g of anhydrous sodium carbonate, and 1.5 g of potassium permanganate in 200 ml of water. A slight turbidity after sodium carbonate dissolution is acceptable. Use the provided 250 ml plastic beaker to hold the solution, which can later be stored in a closed lab container at room temperature for at least one month. Immerse the TLC plate in the solution using tweezers, remove it immediately, let excess solution to run down onto a paper towel, and dry the back of the plate with a tissue. Dry the entire chromatoplate on a hot plate for not more than one minute. Dry the plate carefully to ensure that the spots appear gradually. Observe white spots for ibuprofen becoming visible as the permanganate solution disappears due to oxidation. The process can also be done by spraying the solution and drying with a hairdryer, but both procedures require repeated practice to become perfect. One should observe the entire drying process closely from start to finish. Interim results can sometimes be easier to interpret than the final result. As oxidation continues unabated even after the drying process has been halted, the endpoint is virtually impossible to determine, and all ibuprofen spots continue to grow in size, fray at the edges and become indistinguishable from one another, even if the underlying concentrations differ.

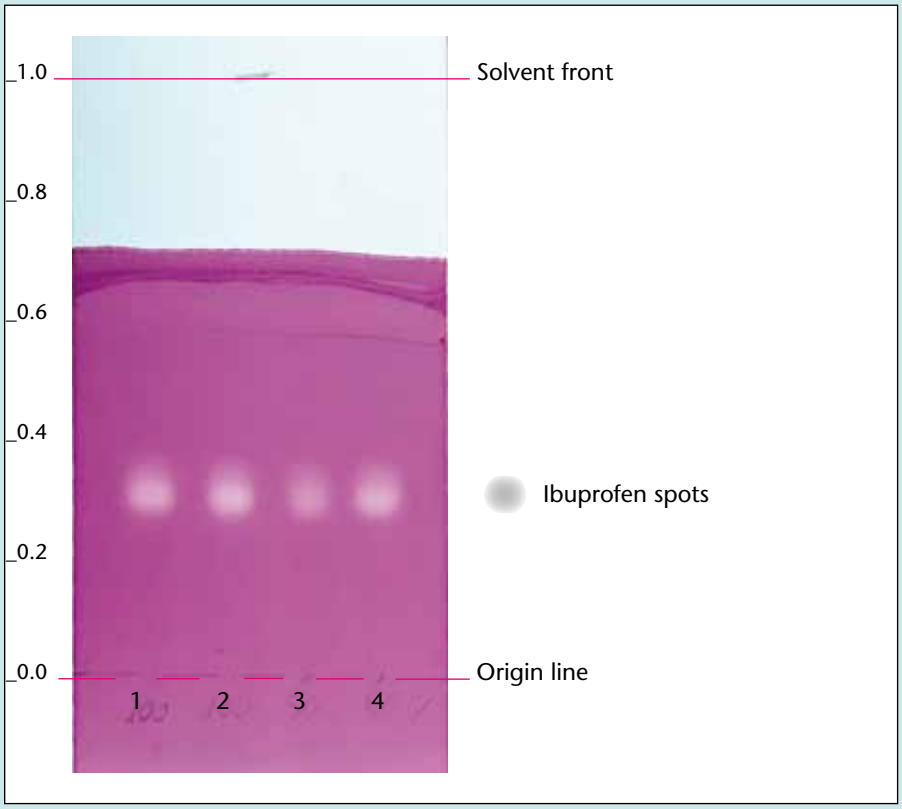
CHROMATOPLATE OBSERVED AT DAYLIGHT AFTER PERMANGANATE STAINING

Run No.1:
Upper working standard representing 100% of total Ibuprofen

Run No.2:
A product of good quality with acceptable ibuprofen content

Run No.3:
A product of poor quality with unacceptable low ibuprofen content

Run No.4:
Lower working standard representing 80% of total ibuprofen



XI. OBSERVATIONS MADE AT DAYLIGHT AFTER PERMANGANATE STAINING

After staining with a permanganate solution, a dark purple background forms. Compounds that react with the visualisation solution turn light yellow to white, making the thin-layer chromatography plate appear like a negative. White spots at a travel distance of approximately 0.33 indicate the presence of ibuprofen. For quantification, ibuprofen spots that form early should preferably be used. Older spots may appear more uniform in size and be more difficult to interpret in terms of ibuprofen content. Other excipients contained in various finished products may produce no spots or only faint ones, migrate towards the solvent front, or remain near the origin.

XII. RESULTS & ACTIONS TO BE TAKEN

The ibuprofen spot in the chromatogram obtained with the test solution must correspond in terms of colour, size, intensity, shape and travel distance to that in the chromatogram obtained with the lower and higher standard solution. This result must be obtained for each method of detection. If this is not achieved, repeat the run from scratch with a second sample. Reject the batch if the drug content cannot be verified in a third run. For a second opinion, refer additional samples to a fully-fledged drug quality control laboratory. Retain samples and put the batch on quarantine until a final decision on rejection or release has been taken. For documentation purposes, take pictures of all the readings with a digital camera.

- Detecting falsified and substandard medicines in low and middle-income countries
- Protecting consumers and medicines supply chains
- Boosting medicines testing capacities for priority medicines
- Assisting in post-marketing medicines quality monitoring
- Complementing the work of existing medicines control laboratories

The GPHF-Minilab™
is a unique miniature laboratory which comes with
affordable test methods for a rapid and easy detection of
falsified and substandard medicines as entry-level technology for
resource limited health settings in low- and middle-income countries.

In more than twenty-five years of project work, the GPHF-Minilab™ has
proven its suitability in more than a 100 countries.

This supplement to the Minilab Manual expands the current list of 125 active
agents to overall 126 active pharmaceutical ingredients now including
also ibuprofen as palliative medicines in self-care.

The final list of 126 active pharmaceutical ingredients for rapid quality
verification of a wide range of finished pharmaceutical products
is joined by a thin-layer chromatographic test for the simple
and rapid testing of antifreeze agents, diethylene
glycol and ethylene glycol, in syrups and other
liquid preparations for oral use.

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