A Concise Quality Control Guide on Essential Drugs and other Medicines

Demo

Manual

Accompanying the GPHF-Minilab™

Review and Extension
2022
now with 107 Test Protocols

Physical Testing & Thin-Layer Chromatography

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PQM Promoting the Quality of Medicines

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is implemented by the U. S. Pharmacopeial Convention (USP).

New test protocols highlighted in yellow

Minilab Test Protocols Sorted by Therapeutic Classes*

Transmissible Diseases

Antibacterials
Amoxicillin
Ampicillin
Azithromycin
Benzathine benzylpenicillin
Benzylpenicillin
Cefalexin
Cefazolin
Cefixime
Cefotaxime
Cefpodoxime
Ceftriaxone
Cefuroxime
Chloramphenicol
Chlorhexidine
Ciprofloxacin
Clarithromycin
Clavulanic acid
Clindamycin
Cloxacillin
Doxycycline
Erythromycin
Gentamicin
Levofloxacin
Metronidazole
Moxifloxacin
Ofloxacin
Phenoxymethylpenicillin
Procaine benzylpenicillin
Sulfamethoxazole/Trimethoprim
Tetracycline

Antimycobacterials
Amikacin
Capreomycin
Cycloserine
Dapsone
Ethambutol
Ethionamide
Isoniazid
Kanamycin
Levofloxacin
Moxifloxacin
Ofloxacin
P-Aminosalicylic acid
Protionamide
Pyrazinamide
Rifampicin
Streptomycin

Antimalarials
Amodiaquine
Artemether
Artesunate
Atovaquone
Chloroquine
Dihydroartemisinin
Doxycycline
Halofantrine
Lumefantrine
Mefloquine
Piperaquine
Primaquine
Proguanil
Pyrimethamine
Pyronaridine
Quinine
Sulfadoxine
Sulfamethoxypyrazine

Anti(retro)virals
Aciclovir
Didanosine
Efavirenz
Indinavir
Lamivudine
Nevirapine
Oseltamivir
Ritonavir
Stavudine
Zidovudine

Anthelminthics
Albendazole
Mebendazole
Praziquantel

Antifungals
Fluconazole
Griseofulvin

Non-Transmissible Diseases

Analgesics
Acetylsalicylic acid
Diclofenac
Mefenamic acid
Naproxen
Paracetamol

Antiallergics
Cetirizine
Chlorphenamine
Dexamethasone
Prednisolone

Antiasthmathics
Aminophylline
Salbutamol

Cardiovascular agents
Amlodipine
Atenolol
Bisoprolol
Captopril
Furosemide
Hydrochlorothiazide
Irbesartan
Lisinopril
Losartan
Methyldopa
Nifedipine
Simvastatin
Telmisartan
Valsartan

Endocrine agents
Clomifene
Glibenclamide
Metformin

Gastrointestinal agents
Metoclopramide
Omeprazole
Ranitidine

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*Usual fixed-dose combinations are included. For full detail on this, see alphabetical order in the table of contents.

New test protocols highlighted in yellow

Table of Contents

** Non-modified, instant soluble tablets and capsules containing the active pharmaceutical ingredient per free base as single agent are forming the baseline for each test protocol by default. Any further inclusion of salt forms, pharmaceutical formulations and fixed dose combination products is named separately. In addition, each protocol includes a number of common dosage strengths.*

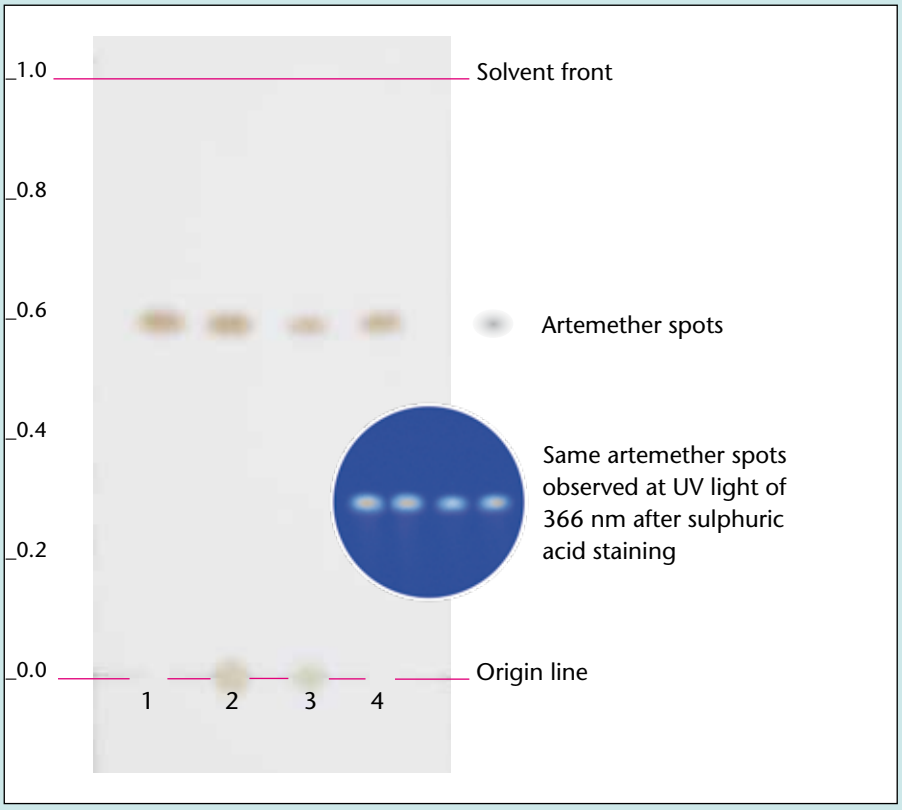
CHROMATOPLATE OBSERVED AT DAYLIGHT AFTER SULPHURIC ACID STAINING

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

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

Run No.3:
A product of poor quality with un-acceptable low artemether content

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



XI. OBSERVATIONS MADE AT 254 NM BEFORE STAINING

Artemether itself stays almost invisible and no other spots should be detected unless the medicine under investigation is presented as a co-formulated product. In the latter case, a strong violet spot at a travel distance of about 0.20 indicates the presence of lumefantrine and, in case of dry powders for oral suspensions, a second strong spot between a travel distance of 0.40 and 0.50 indicates the presence of a preservative either from the benzoate or paraben family. Saccharin sodium as sweetener in dispersible tablets would settle at about 0.20 but stays below its limit of detection due to strong dilutions during sample preparation. For a better identification of the lumefantrine fraction go to 286 of this manual.

XII. OBSERVATIONS MADE AT DAYLIGHT AFTER SULPHURIC ACID STAINING

A dark brown spot at a travel distance of about 0.58 indicates the presence of artemether in the test solution. Auxiliary agents incorporated in the different tablet and powder formulations may cause further spots near or on the origin line. Beyond this, no other spots should be visible even if artemether is combined with lumefantrine. Additional strong spots generated by the test solution would point at other drugs or artemether degradation, the latter case being more likely when associated with a smaller principal spot. A smaller principal spot from the test solution may also indicate a poor artemether content and no spot at all a complete artemether absence.

XIII. OBSERVATIONS MADE AT 366 NM AFTER SULPHURIC ACID STAINING

When exposing the chromatoplate to UV light of 366 nm after heating with sulphuric acid, all brown artemether spots previously observed at daylight are now showing an off-white fluorescence.

XIV. RESULTS & ACTIONS TO BE TAKEN

The artemether 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 some 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 turning off the flash first.

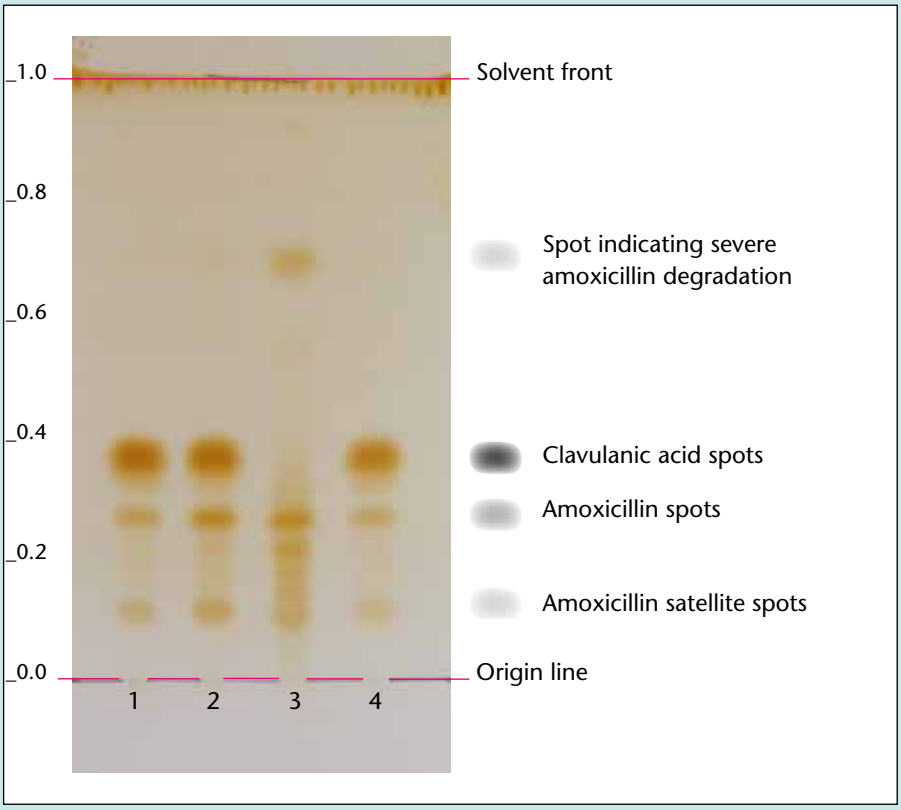
CHROMATOPLATE OBSERVED AT DAYLIGHT AFTER IODINE STAINING

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

Run No.2:
A fixed-dose combination product of good quality with acceptable clavulanic acid content

Run No.3:
A fixed-dose combination product where clavulanic acid is missing and amoxicillin degrading

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



XI. OBSERVATIONS MADE AT 254 NM

Clavulanic acid stays invisible and spots at a travel distance of about 0.28 indicate the presence of amoxicillin in the test solution. Additional strong spots generated by the test solution would point at other drugs. For a further verification of amoxicillin identity and content follow the relevant protocol shown in this manual.

XII. OBSERVATIONS MADE AT DAYLIGHT AFTER IODINE STAINING

A strong yellow-brown spot at a travel distance of about 0.38 indicates the presence of clavulanic acid in the test solution. Amoxicillin spots already observed at 254 nm are now turning yellowish brown, too. Additional strong spots generated by the test solution would point at other drugs or some degradation of clavulanic acid or amoxicillin, the latter case being more likely when each time associated with a smaller principal spot. A smaller principal spot from the test solution may also indicate a poor clavulanic acid content and no spot at all a complete absence of clavulanic acid. Still observe the plate when iodine evaporates. Spots reflecting poor quality products will disappear first gradually followed by the reference spots representing a drug content of an 80 and 100 percent, respectively. Auxiliary agents incorporated in different finished products might cause some fainter spots either travelling alongside the solvent front or emerging near or on the origin line.

XIII. RESULTS & ACTIONS TO BE TAKEN

The spot for clavulanic acid 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 turning off the flash first.

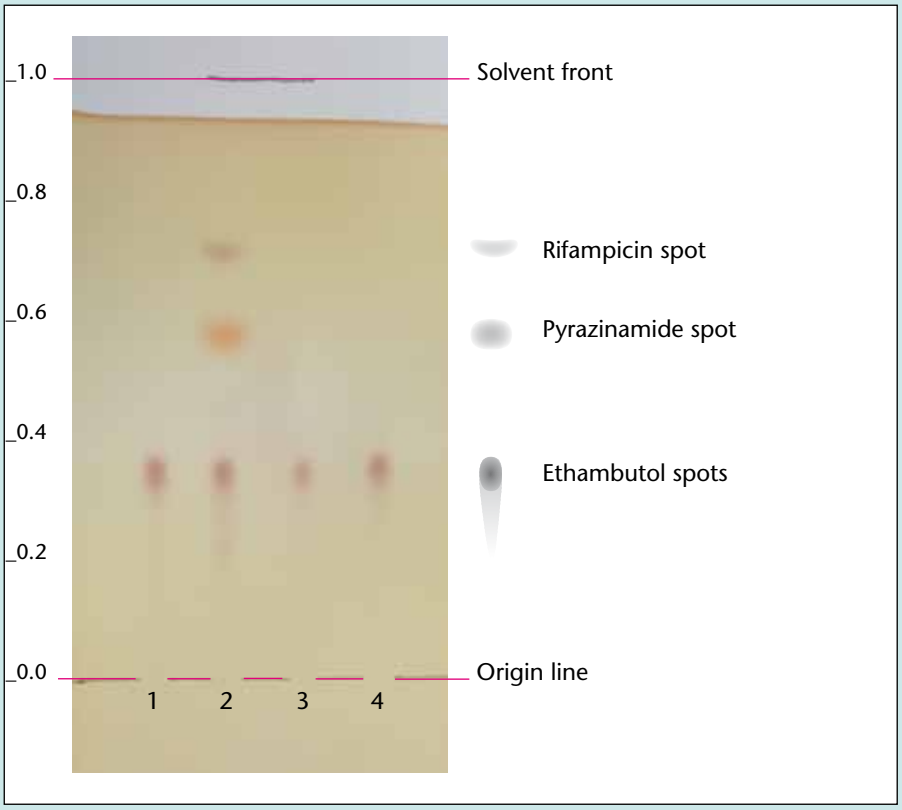
CHROMATOPLATE OBSERVED AT DAYLIGHT AFTER NINHYDRIN STAINING

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

Run No.2:
A fixed-dose combination product of good quality with acceptable ethambutol content

Run No.3:
A single drug product of poor quality with unacceptable low ethambutol content

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



XI. OBSERVATIONS MADE AT 254 NM

Ethambutol stays invisible and no other spots should be detected unless the medicine under investigation is presented as a fixed-dose combination product containing also other antituberculosis compounds. In the latter case, spots made of isoniazid will become visible at a travel distance of about 0.45 and spots made of pyrazinamide at a travel distance of about 0.57. Spots made of rifampicin will be visible at a travel distance of about 0.72 at daylight already. For all of this, consult also the picture shown on page 405.

XII. OBSERVATIONS MADE AT DAYLIGHT AFTER STAINING WITH NINHYDRIN

A red spot at a travel distance of about 0.34 indicates the presence of ethambutol in the test solution. Next to ethambutol, rifampicin and pyrazinamide will be become visible, too. Additional strong spots generated by the test solution would point at other drugs or ethambutol degradation, the latter case being more likely when associated with a smaller principal spot. A smaller principal spot from the test solution may also indicate a poor ethambutol content and no spot at all a complete ethambutol absence. Auxiliary agents incorporated in different finished products might cause some fainter spots either travelling alongside the solvent front or emerging near or on the origin line.

XIII. RESULTS & ACTIONS TO BE TAKEN

The ethambutol 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 turning off the flash first.

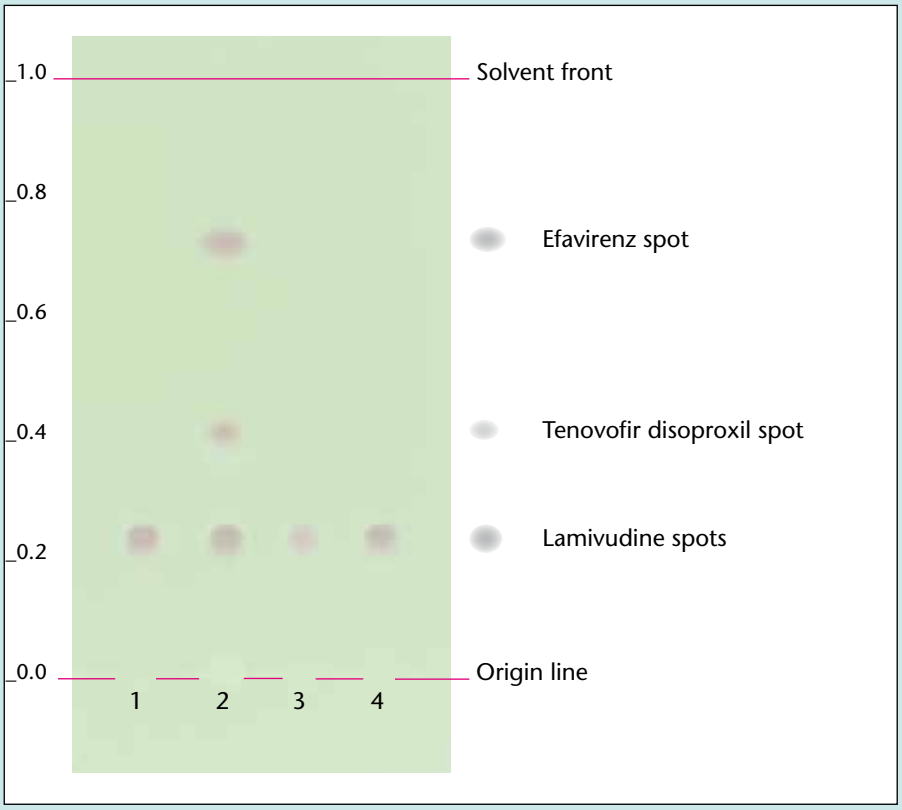
CHROMATOPLATE OBSERVED UNDER UV LIGHT OF 254 NM

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

Run No.2:
A fixed-dose triple combination product of good quality with acceptable lamivudine content

Run No.3:
A single drug product of poor quality with unacceptable low lamivudine content

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



X. DETECTION

Dry off all residual solvent and observe the chromatoplate under UV light of 254 nm using the battery-driven lamp supplied. Use this method of detection for both, identification and quantification purposes.

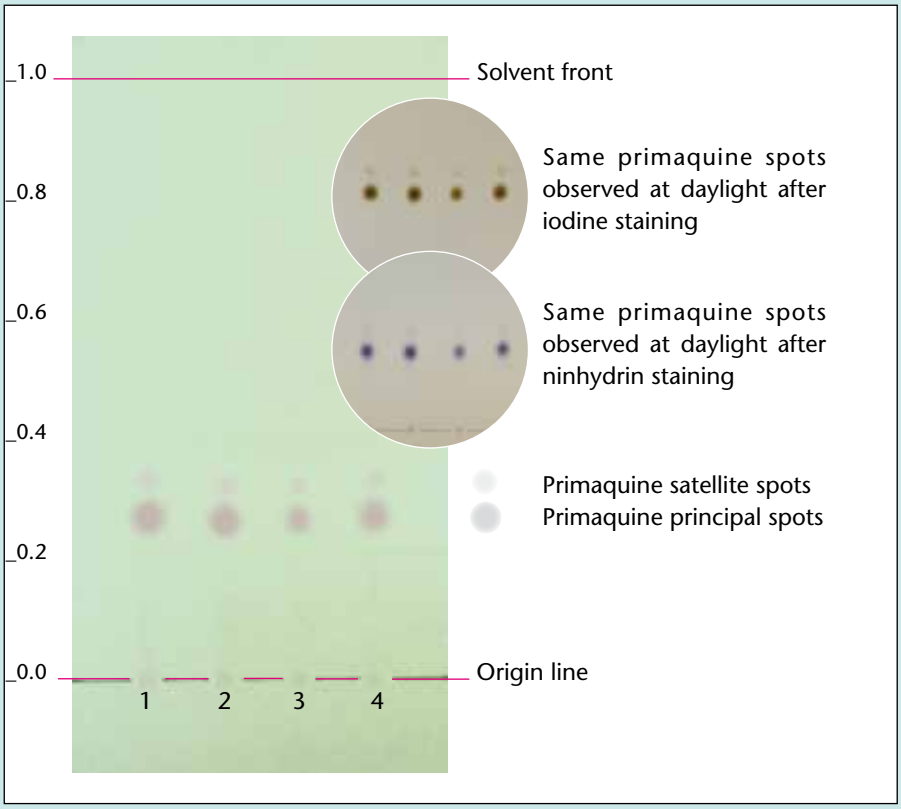
XI. OBSERVATIONS MADE AT 254 NM

A strong blue-violet spot at a travel distance of about 0.23 indicates the presence of lamivudine in the test solution. If combined with other antiretroviral medicines, a spot with a relative retention factor of about 0.42 would further indicate the presence of tenofovir disoproxil, a spot at about 0.62 the presence of nevirapine or zidovudine and a spot at about 0.72 the presence of efavirenz. Additional strong spots generated by the test solution would point at other drugs or lamivudine degradation, the latter case being more likely when associated with a smaller principal spot. A smaller principal spot could also be due to a poor lamivudine content and no spot at all due to a complete lamivudine absence. Auxiliary agents incorporated in different finished products might cause some fainter spots emerging near or on the origin line.

XII. RESULTS & ACTIONS TO BE TAKEN

The lamivudine 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 a picture of the reading with a digital camera turning off the flash first.

CHROMATOPLATE OBSERVED UNDER UV LIGHT OF 254 NM



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

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

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

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

XI. OBSERVATIONS MADE AT 254 NM

A strong blue-violet spot at a travel distance of about 0.27 combined with a smaller satellite spot just above the principal spot indicates the presence of primaquine in the test solution. Additional strong spots generated by the test solution would point at other drugs or even primaquine degradation, the latter case being more likely when associated with a smaller principal spot. A smaller principal spot from the test solution may also indicate a poor primaquine content and no spot at all a complete primaquine absence.

XII. OBSERVATIONS MADE AT DAYLIGHT AFTER IODINE STAINING

When exposing the chromatoplate to iodine vapour, all spots already observed at 254 nm are now turning greenish black. Primaquine performs strong here and the colour stays stable. Auxiliary agents incorporated in different finished products might cause some fainter spots either travelling alongside the solvent front or emerging near or on the origin line.

XIII. OBSERVATIONS MADE AT DAYLIGHT AFTER NINHYDRIN STAINING

When exposing a second chromatoplate to ninhydrin and heat, then all primaquine spots previously observed at UV light of 254 nm are now turning lilac. This will facilitate further assay reading and interpretation.

XIV. RESULTS & ACTIONS TO BE TAKEN

The primaquine 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 turning off the flash first.

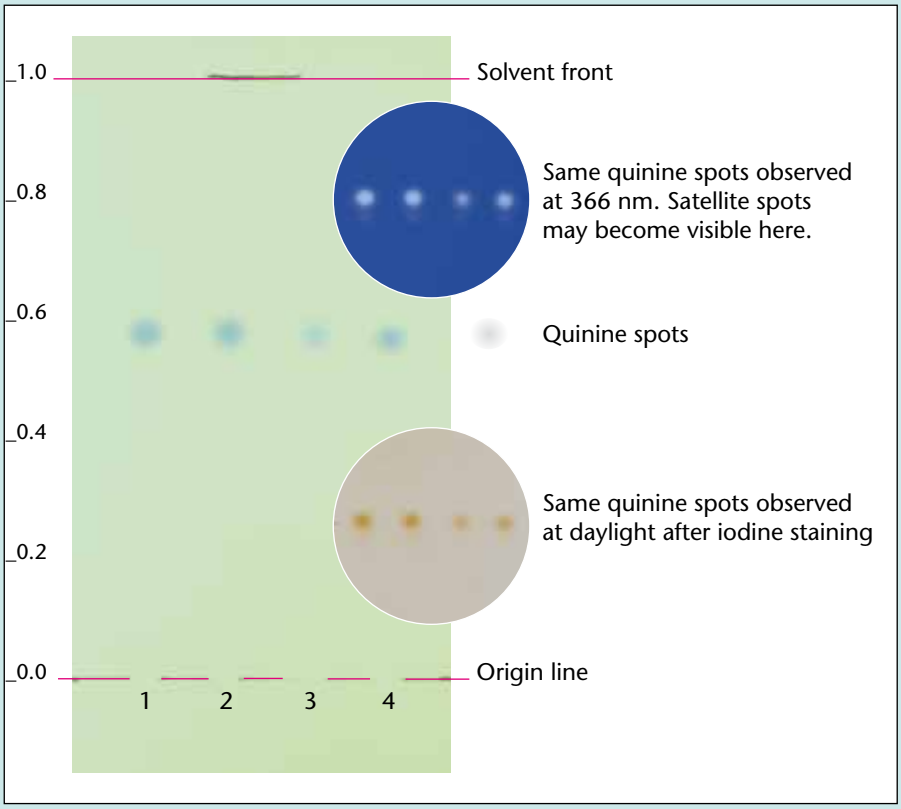
CHROMATOPLATE OBSERVED UNDER UV LIGHT OF 254 NM

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

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

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

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



XI. OBSERVATIONS MADE AT 254 NM

A strong blue spot at a travel distance of about 0.59 indicates the presence of quinine in the test solution. Additional strong spots generated by the test solution would point at other drugs or quinine degradation, the latter case being more likely when associated with a smaller principal spot. A smaller principal spot from the test solution may also indicate a poor quinine content and no spot at all a complete quinine absence. Auxiliary agents incorporated in different finished products might cause some fainter spots either travelling alongside the solvent front or emerging near or on the origin line.

XII. OBSERVATIONS MADE AT 366 NM

On exposer to 366 nm in a dark room, the blue fluorescence observed for the quinine spots at 254 nm will now turn into an intense white fluorescence. In addition, under ideal detection conditions, a minor satellite spot probably arriving from dihydroquinine will now become visible just below each quinine spot. The latter observation will further emphasise the existence of quinine in the test solution.

XIII. OBSERVATIONS MADE AT DAYLIGHT AFTER IODINE STAINING

When exposing the chromatoplate to iodine vapour, all quinine spots already observed at 254 and 366 nm are now turning orange-brown. Still observe the plate when iodine evaporates. Spots reflecting poor quality products will disappear first gradually followed by the reference spots representing a drug content of an 80 and 100 percent, respectively.

XIV. RESULTS & ACTIONS TO BE TAKEN

The quinine 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 the readings with a digital camera turning off the flash first.

CHROMATOPLATE OBSERVED UNDER UV LIGHT OF 254 NM

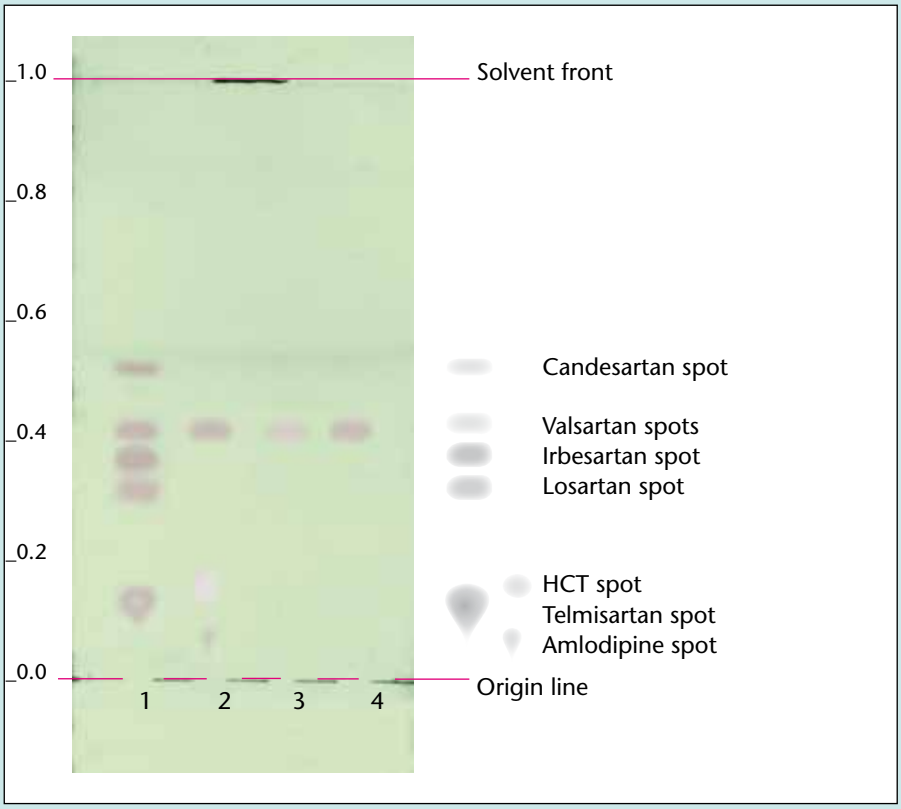
Run No.1:
Upper working standard representing 100% of total valsartan

Also showing that the selected mobile phase is specific, other sartans were added to the standard solution

Run No.2:
A fixed-dose triple combination product of good quality with acceptable valsartan content

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

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



line of origin. When hydrochlorothiazide (HCT) is combined with valsartan in a favourable ratio, under ideal conditions a very faint HCT spot may appear at a travel distance of about 0.15 below the valsartan spot. In reverse cases, due to strong dilutions, the HCT concentration will drop below its limit of detection. If combined with amlodipine, a tiny spot is visible at a travel distance of about 0.06 near the line of origin. For triple fixed-dose combination products, three spots for valsartan, HCT and amlodipine can be observed under ideal conditions. In order to show that the selected mobile phase is specific for many sartans, candesartan (R_f = 0.53), irbesartan (R_f = 0.35), losartan (R_f = 0.29) and, telmisartan (R_f = 0.12) were added to the reference solution as seen above on run number one.

XII. OBSERVATIONS MADE AT 366 NM

When valsartan is combined with amlodipine, the presence of the latter compound is confirmed by a strong white fluorescence at a travel distance of about 0.06 very close to the origin line.

XIII. RESULTS & ACTIONS TO BE TAKEN

The valsartan 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 turning off the flash first.

- 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 years of project work, the GPHF-Minilab™ has proven
its suitability in up to a 100 countries.

A comprehensive review of the Minilab's general methods and operations and
its test protocols drawn from the main manuals issued 1998, 2008 and 2020
including their many extensions issued each year.

Topped with testing protocols for more active pharmaceutical ingredients
listed as priority medicines for the treatment of communicable and
non-communicable diseases, this new manual now provides
simple testing procedures for 107 active pharmaceutical
ingredients for rapid and economical drug quality
verification of a wide range of finished
pharmaceutical products.

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