Institut für Pharmazeutische Chemie der Philipps-Universität, Marburg, Germany

Colour reactions of griseofulvin Ph. Eur. 2005 using hydrogen peroxide solution or bromate or iodate as oxidant instead of potassium dichromate

Analytical methods in respect to environmental and economical concern Part 22*

M. HILP

Received July 26, 2005, accepted August 30, 2005

Priv.-Doz. Dr. Manfred Hilp, Haselhecke 42, D-35041 Marburg, Germany
manfred@hilp.de

Pharmazie 61: 74 (2006)

Ph. Eur. 2005 identifies griseofulvin in a colour reaction using toxic, and carcinogenic potassium dichromate as oxidant, which is hazardous for the environment. It is recommended to apply non toxic hydrogen peroxide solution or bromate or periodate.

Ph. Eur. 2005 uses potassium dichromate as oxidant for the colour reaction to identify glycerol, griseofulvin, isopropyl alcohol, magnesium peroxide, mefenamic acid, paracetamol, pilocarpine hydrochloride, pilocarpine nitrate, sodium perborate, and sodium picosulfate. Also warfarin sodium and warfarin sodium clathrate are distinguished by reduction of dichromate in nitric acid. Furthermore, potassium dichromate in sulphuric acid is applied as spray reagent for TLC in the monographs of calcium gluconate, chlorhexidine digluconate solution, clomipramine hydrochloride, desipramine hydrochloride, ferrous gluconate, imipramine hydrochloride, methyltestosterone, and trimipramine maleate. For the identification of iodides (2.3.1. method b) dichromate is applied in the monographs of potassium and sodium iodide.

However, potassium dichromate is a toxic, and carcinogenic reagent, which is hazardous for water (http://www.carl-roth.de; http://www.chemdat.merck.de; http://www.chemie.fu-berlin.de).

As shown in the Table, in the colour reaction of griseofulvin Ph. Eur. 2005, forming a wine-red coloured o-quinone (Auterhoff and Kliem 1976) potassium dichromate can be replaced by environmentally safer and less toxic hydrogen peroxide solution, potassium bromate or sodium periodate. 1,3-Dibromo-5,5-dimethylhydantoin (DBH) is unsuitable.

Experimental

1. Materials

Griseofulvin [126-07-8], minimum 95% (hplc), penicillium griseofulvum, Sigma®, art. G4753, hydrogen peroxide solution 30% [7722-84-1], medically extra pure, stabilized, Ph. Eur., BP, USP, Merck art. 108597, potassium bromate [7758-01-2], reag. Ph. Eur., Merck art. 159199, potassium dichromate [7778-50-9], reag. Ph. Eur., Merck art. 159207, sodium periodate, sodium metaperiodate [7790-28-5], reag. Ph. Eur., Merck art. 159321, sulphuric acid [7664-93-9], p. a. conc., 95–97%, Riedel-deHaën art. 30743.

2. Solutions

see Hilp (2002).

3. Colour reactions

According to Ph. Eur. 2005, 5 mg of griseofulvin are dissolved in 1 ml of sulphuric acid and treated with oxidants as described in the Table.

Acknowledgements: The author acknowledges Mrs. H. Yanardag for experimental performance.

*Part 21: Hilp M (2004)

References

Auterhoff H, Kliem M (1976) Die Nachweisreaktion von Griseofulvin mit Kaliumdichromat in Schwefelsäure. Arch Pharm (Weinheim) 309: 326–329.

Hilp M (2002) Colour reactions of PH. EUR. for identification of drugs using 1,3-dibromo-5,5-dimethylhydantoin (DBH) instead of elemental bromine; analytical methods of pharmacopoeias with DBH in respect to environmental and economical concern Part 10. Pharmazie 57: 172–175.

Hilp M (2004) Determination of peroxide values using ethyl acetate as solvent; analytical methods in respect to environmental and economical concern Part 21. Pharmazie 59: 721–722.

Table: Reaction of griseofulvin with various oxidants (5 mg in 1 ml of sulphuric acid)

Oxidant	Colour	Blind value (without griseofulvin)
$K_2Cr_2O_7$		
5 mg according to Ph. Eur. 2005	wine-red, after 10 min brownish yellow	
H_2O_2		
3% two drops	only orange	colourless
30% two drops	orange, changing immediately to wine-red	colourless
DBH		
0.2 ml 0.05 M–DBH/0.5 M–NaOH	yellow	
0.5 ml 0.05 M–DBH/0.5 M–NaOH	yellow ↓	
2.0 ml 0.05 M–DBH/0.5 M–NaOH	yellow ↓	
0.2 ml 0.05 M–DBH/HAc	yellow	
0.2 ml 0.05 M–DBH/HAc	yellow	
0.2 ml 0.05 M–DBH/HAc	yellow	
5 mg DBH	orange, after 10 min orange and turbid	
$KBrO_3$		
shaking with 5 mg	immediately wine-red	orange
$NaIO_4$		
slowly soluble in sulphuric acid, shaking with 5 mg	wine-red	colourless