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Stability-indicating high-performance liquid chromatographic assay methods for drugs in pharmaceutical dosage forms: Part I

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Stability-Indicating High-Performance Liquid Chromatographic Assay Methods for Drugs in Pharmaceutical Dosage Forms: Part II

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BRIEF SUMMARIES(CONTINUED)

This article is the second of two parts. Part I appeared previously in the December(1996) issue. In Part II, we continue the summaries of the remaining references selected by the authors.

XIV. *Beta-adrenoceptor Blocking Agents*

A stability-indicating HPLC assay of propranolol for transdermal permeation study was described by Tenjarla and Chow(97). The calibration graphs were linear for 0.5-10 and 1-15μg/mL of propanolol in PBS diffusate and skin extract, respectively. Low within-day (2.2 and 8.8% for diffusate and skin extract, respectively) and between-day (2.2 and 7.7%, respectively) RSD were obtained. The method was used to study the transdermal permeation of propanolol.

Aqueous solutions of esmolol hydrochloride, methyl 3-{4-[2-hydroxy-3- (isopropylamino) propoxy]phenyl}propionate, containing 2-(4-chlorophenyl)-2-methylpropanol as internal standard, were analyzed by Lee et al. (98). The stability-indicating nature of the HPLC method was demonstrated by separating esmolol from synthetic intermediates, potential impurities and decomposition products.

XV. *Chelating Agents Antidotes and Antagonists*

Schroeder et al. (99) separated Pralidoxime chloride from its decomposition products by HPLC. It was found that solutions containing 300 mg/mL of the cited drug stored for 8 to 10 years at room temperature followed by 3 to 4 years at 5 °C still contained >90% of the original amount of the drug.

An HPLC method has been developed for the separation and determination of pralidoxime chloride, its precursor picolinaldoxime and other structurally related compounds (including decomposition products) by Prue et al. (100). The method was successfully applied in a study of the stability of an injectable formulation; a decomposition product of unknown composition was detected.

XVI. *Hormonal Contraceptives*

Chi et al. (101) reported an HPLC assay of gossypol acetate in male contraceptive tablets. The method showed that gossypol acetate was unstable in ethanolic solution, and, to a lesser extent, in acetone, benzene, $CHCl_3$ and ethyl acetate.

Reif et al. (102) reported an automated stability-indicating HPLC assay for ethinyloestradiol and norgestrel or levonorgestrel in oral contraceptive tablets. Ethinyloestradiol and norgestrel or levonorgestrel can be well separated from excipients, impurities and degradation products. The sample injection system was under computer control. The method is applicable for content uniformity and stability testing at a rate of 8 samples per hour.

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XVII. *Corticosteroids*

The stability of triamcinolone acetonide in aqueous ethanol solution at pH 1.6 to 12 with varying buffer concentrations and ionic strengths and in polyoxyethylene glycol-based ointment was studied by Das-Gupta [103]. The decomposition pathway of triamcinolone acetonide is discussed.

HPLC studies on the stability of hydrocortisone sodium succinate in the presence of aminophylline in some infusion fluids was described by Stoberski et al. [104]. The results obtained were compared with those from the extraction method of Anderson and Latiolais (Am. J. Hosp. Pharm., 1970, 27: 540) and statistically evaluated; the HPLC technique was more precise. The stability of hydrocortisone sodium succinate according to its concentration and pH value of the solution is discussed.

Zakrzewski et al. [105] examined Fenicort [prednisolone sodium tetrahydrophthalate] stability in some intravenous solutions by HPLC. The results obtained and the pH values of infusion solution used are tabulated and statistically compared with the results obtained by spectrophotometric determination of Fenicort at 246 nm after extraction of the decomposition products of Fenicort with $CHCl_3$. The HPLC procedure was found to be faster and more precise.

Bachman and Gambertoglio [106] described a stability-indicating HPLC assay for prednisolone sodium phosphate in implantable infusion pumps. It was reported that good separation of prednisolone sodium phosphate from formulation excipients, impurities and breakdown products was achieved. The method was used to monitor stability in implantable infusion pumps; results show that prednisolone sodium phosphate is stable at 37°C for at least 3 weeks.

Smith and Haigh [107] developed a highly efficient HPLC procedure for the determination of betamethasone valerate in isopropyl myristate solution formed as the receptor phase of in vitro diffusion cells. Slight modification allows for the determination of other corticosteroids.

A rapid HPLC analysis and stability study of hydrocortisone 17-butyrate in cream preparations was reported by Wanwimolruk [108]. The described HPLC method is shown to be selective in separating the intact drug from its decomposition products and product excipients.

XVIII. *Cough Suppressants Expectorants and Mucolytics*

S-carboxymethylcysteine [carbocisteine] in syrup formulations was determined by Melucci et al. [109]. HPLC was used to investigate the stability of the drug. Results showed that the degradation products of carbocisteine did not interfere.

XIX. *Dental*

α -ionone in toothpaste was determined by Trivedi [110] using HPLC. The proposed method could be applied to study the stability of the cited drug in toothpaste products.

XX. *Dermatological Agents*

Dithranol and its degradation products danthron and dianthrone were determined in the bulk drug and in ointments by Albert [111]. The method was stability-indicating, and the coefficient of variation was 0.7%.

Pavelek and Benes [112] determined allantoin in dosage forms containing a complex of iodine with polyvinylpyrrolidone. The method was found useful to study the stability of allantoin preparations. Some other HPLC procedures were developed by Yamamoto et al. [113] for the determination of allantoin and the identification of its degradation compounds. The methods were used to study the stability of allantoin in buffers of pH 3, 6 and 9 for 55 days at 50°C. And Trivedi [114] determined allantoin in cosmetic lotion. The HPLC method was applied for stability study and the recovery from samples spiked with decomposition products was 99.8%.

XXI. *Disinfectants*

Pharmaceutical preparations containing noxythiolin were analyzed by Irwin et al. [115] using a stability-indicating HPLC method. The

stability of the cited drug was studied in this work.

XXII. *Diuretics*

Mensink et al. [116] developed an HPLC procedure to determine tretinoin in pharmaceutical. It was found that the cited drug was best determined by the method which was applied to the stability studies of the drug.

Hitscherich et al. [117] simultaneously determined hydrochlorothiazide and propranolol hydrochloride in tablets using HPLC. Impurities, degradation products and excipients do not interfere, and the method can be used to study the stability of propranolol hydrochloride.

Frontini and Mielck [118] separated bendroflumethiazide (bendrofluazide) from its degradation products [its 3-debenzyl analogue and 5-trifluoromethyl-2,4-disulfamoylaniline] using HPLC. To ensure stability, samples must be stored in the dark and dissolved in aqueous methanol at pH 2. Perlman et al. [119] analyzed bendrofluazide and nadolol in combination tablet formulations using HPLC. The stability of bendrofluazide was confirmed by observing no change in the disulfonamide content after 60 h. The increase in the content of degradation products was noted under condition of exposure to light.

Frusemide and hydrocortisone sodium succinate were determined in injection solutions containing glucose and NaCl after storage for 0, 3, 6 or 24 h at 25°C by Stoberski et al. [120]. In their report, the effect of storage on their stability was discussed.

Bauer et al. [121] found that acidic degradation of chlorthalidone in tablets occurred during assay preparation to form small amounts of 2-(3-aminosulphonyl-4-chlorobenzoyl)benzoic acid and 3-[(4-chloro-3- aminosulphonyl)phenyl]-1H-isoindol-1-one. All three compounds can be separated and determined by HPLC.

XXIII. *Dopaminergic Antiparkinsonian Agents*

Shen and Ye [122] determined the stability of dopamine in aqueous solutions by HPLC. It was found that the solution was stable in acid but dopamine was rapidly oxidized in a neutral solution, with EDTA giving partial protection. The chromatograms gave evidence of further oxidation beyond the quinone stage. These results are of importance in the handling of large numbers of dopamine extracts.

α -methyldopa in sustained-release capsules was determined by El-Sayed-Metwally [123] using HPLC. It was reported that the separation of the drug substance from the industrial impurity 3-(O-methyl)methyldopa was good. Kafil and Dhingra [124] described a stability-indicating HPLC assay for the determination of levodopa, levodopa-carbidopa and related impurities in pharmaceutical preparations. The intra-day RSD was 1.5-2% and the inter-day RSD (n = 6) was 2% for levodopa and 1.6% for carbidopa.

XXIV. *Ergot Alkaloids and Derivatives*

Dihydroergotamine mesylate in tablet form was determined by Tokunaga et al. [125]. The HPLC method was also applied to a study of the stability of dihydroergotamine (0.2 mg/mL) in aqueous 1% tartaric acid under various conditions.

XXV. *Gastro-intestinal Agents*

Tablets containing the antispasmodic agent mebeverine hydrochloride were assayed by De-Schutter et al. [126]. The system separates three degradation products, N-ethyl-N-[2-(4-methoxyphenyl)-1-methylethyl]-4-aminobutanol, methyl veratrate, and veratric acid, and two intermediate compounds from the synthesis, 4-iodobutyl veratrate and N-ethyl-1-(4-methoxyphenyl)isopropylamine, as well as other antispasmodic agents. Degradation products were also identified by m. s. The tablets were stable at 50°C for over a year, after which 96.8% of active substance was measured.

Parasrampuria and Das-Gupta [127] quantitated famotidine in tablets or suspensions using HPLC. Chromatograms for samples subjected to drastic acid or base decomposition yielded up to three extra peaks. Salem et al. [128] developed

another HPLC method which was used in studies of dissolution and of stability of famotidine in tablet formulation. The determination of famotidine in tablet form was also carried out by Suleiman et al. [130]. It was reported that within-day coefficients of variation (n = 6) were 2.2 and 0.82% at 2.5 and 10 mg/L, respectively. The day-to-day coefficients of variation (n = 6) was 4.7%.

Fatmi and Williams [129] quantitated metoclopramide in tablet dosage forms. The stability-indicating HPLC method can separate the drug from its related compounds, viz. , 4-acetylamino-5-chloro-N-[2-(diethylamino)ethyl]-2-methoxybenzamide and 4-amino-5-chloro-2-methoxybenzoic acid in quantities of up to 10μg/mL. Suleiman et al. [131] reported an HPLC procedure for the determination of metoclopramide hydrochloride in pharmaceutical dosage forms. It was found that the within-day coefficients of variation were 1.7, 0.5 and 0.9%, respectively (n = 6), with corresponding between-day values of 3.6, 4.1 and 0.7%.

The H_2 blocker ranitidine was determined by Hoyer et al. [132] using a sensitive stability indicating assay. The HPLC method separated ranitidine from its main degradation product, ranitidine-S-oxide and from two other unknown degradation products, and could be used for stability studies.

XXVI. *Hepatotonics*

Bauer et al. [133] analyzed tin protoporphyrin and other free-acid metalloporphyrins by HPLC. The method was applied to the assessment of stability of the aqueous solution of the cited drug.

XXVII. *Hypothalamic and Pituitary Hormones*

Buck et al. [134] reported an HPLC method in which the analysis of ornipressin was carried out at 60°C or 80°C. This method was compared with B. P. lypressin biological assay performed on live rats. It was found that ornipressin was well separated from other peptides, including lypressin, by HPLC at 80°C, and results by the two methods were well correlated (r = 0.9998). The HPLC method shows the better precision and is considered to be suitable for estimating the potency of the drug and for stability testing of pharmaceuticals.

Protirelin (thyrotrophin-releasing hormone) and benzyl alcohol in a multidose injectable formulation were determined by Subba-Rao et al. [135] using an HPLC procedure which was stability-indicating.

XXVIII. *Local Anaesthetics*

Procaine hydrochloride in aqueous systems were analyzed by Wang of NDMC [136]. It was reported that assay for procaine is carried out by HPLC and no extraction procedure is required. Stability studies were conducted at up to 90°C over periods of 35 days, at various pH values, and with different vehicles. The most stable medium was propane-1,2-diol-ethanol-H_2O (4:1:5) from which approximately 97% of procaine hydrochloride could be recovered after 35 days at 70°C.

Torok et al. [137] determined adrenaline in injections containing a 1000-fold excess of procaine. It was reported that four unidentified degradation products were separated from the drug substance.

XXIX. *Muscle Relaxants*

Fenoverine is a modulator of smooth muscle motility. Hu of NDMC and his co-workers [138] described an HPLC procedure to determine the fenoverine in drug capsules and in human plasma. The application to dosage form stability and pharmacokinetic studies are also presented.

XXX. *Nutritional Agents and Vitamins*

Paveenbampen et al. [139] determined folic acid in multivitamin preparations using a reversed phase HPLC, demonstrating stability indicating effectiveness.

The purity and stability on storage of L-ascorbic acid samples were determined by Kennedy et al. [140] by use of reversed-phase HPLC. Known precursors and oxidation products of ascorbic acid were absent, and so the anaerobic degradation of dry ascorbic acid in sealed containers is suspected. Kmetec [141] simultaneously

determined acetylsalicylic, salicylic, ascorbic and dehydroascorbic acid in capsule form by HPLC. In his work, it was found that detection limits were $\leqq$ 2.0 μ g/mL and can be improved by adjusting the wavelength of UV detection and the sensitivity setting of the fluorescence monitor.

Caviglioli et al. [142] described an HPLC assay for retinoic acid in hard gelatine capsules containing lactose and as bulk drug substance. The authors had successfully employed the assay procedure for more than one year and a half in a stability study and the results of accuracy and precision were good.

Sisco et al. [143] reported an HPLC assay for fenretinide in soft gelatin capsules and concentrated corn oil suspensions. The potential decomposition products retinoic acid, 4-aminophenol and 13-cis-fenretinide also showed a rectilinear response. Treatment of capsules overnight at 100 °C resulted in a decrease in the fenretinide content to approximately 80%. Exposure to light showed a similar effect. In another report, Sisco and DiFeo [144] determined fenretinide [N-(4-hydroxyphenyl)retinamide] and two of its impurities (retinoic acid and the 13-cis-isomer of the drug substance) in aqueous 75% acetonitrile solution. HPLC was used to monitor the thermal stability of the drug samples after heating for 1 month at 60°C and 80°C. Column performance remained steady during many months of heavy use.

XXXI. *Ophthalmic Products*

Thiomersal and chlorhexidine gluconate were determined simultaneously by Hu et al. of NDMC [145] using HPLC. The method was applied in stability studies. Excellent results were obtained. Chlorhexidine digluconate and its breakdown product 4-chloroaniline were determined by Richard et al. [146] using HPLC. The method was found suitable for stability studies of ophthalmic preparations and antiseptic contact-lens solution and is specific; no other common eye-drop ingredients interfered.

Separation of pilocarpine from isopilocarpine, pilocarpic acid and isopilocarpic acid was achieved by Unlu et al. [147]. HPLC was applied in stability studies of ophthalmic solution.

Naphazoline and tetrahydrozoline in ophthalmic preparations were separated by Bauer and Krogh [148]. The method described permits direct analysis of a variety of ophthalmic solutions. Both naphazoline and tetrahydrozoline can be separated from their degradation products. Andermann and Richard [150] reported an HPLC procedure for the separation of tetrahydrozoline hydrochloride and its possible decomposition product N-ethylamino-1,2,3,4-tetrahydro-1-naphthamide in ophthalmic solutions. Results were highly reproducible (RSD = 1.5%). Each of inter-analyst variations, with three different chemists, gave rectilinear results.

Dipivefrine hydrochloride and its two degradation products 3- and 4-monopivaloylepinephrine can be simultaneously monitored by a routine HPLC method developed by Wall et al. [149].

The determination of benzalkonium chloride in phenylephrine HCl 10% ophthalmic solution was reported by Parhizkari et al. [151]. The benzalkonium chloride content was determined from the sum of the individual C12 and C14 homologous peaks. Their method was used to study the effects of heat, acids, bases and UV radiation on the stability of the ophthalmic solution.

Bauer et al. [152] described an HPLC assay for disodium EDTA in ophthalmic preparations. The proposed HPLC procedure was highly reproducible (RSD = 0.6%) and the EDTA response was linear (r = 0.99999) in the range of 0.2 to 2.1 mg/mL. EDTA in ophthalmic preparations can be directly analyzed without being derivatized or converted to an iron complex prior to analysis.

XXXII. *Opioid Analgesics*

Wu et al.[153] of National Narcotics Bureau, Department of Health in Taiwan developed a specific HPLC method to separate morphine from its degradation products, such as pseudomorphine, morphine N-oxide and other highly degraded components. HPLC can be used for the stability and kinetic studies of morphine. In a subsequent

report, Wu et al. [154] described that an HPLC method they developed for the analysis of morphine could separate morphine from its degradation products, such as pseudomorphine and morphine N-oxide, and atropine and its degradation products, such as tropic acid, did not interfere with the assay. In addition, the HPLC method for atropine is capable of separating atropine from its degradation products resulting from hydrogen peroxide-, acid-, base- and photo-stress. Morphine, pseudomorphine and morphine N-oxide did not interfere with the assay. The application of the proposed methods in accelerated stability tests of morphine-atropine injections, which were divided into groups and stored at 40, 60, and 80°C, predicted tentative shelf-lives of 5.4 and 3.6 years for morphine HCl and atropine sulfate, respectively.

The hydrolysis and oxidation of meperidine hydrochloride can result in decomposed products, such as meperidinic acid, meperidine N-oxide and normeperidine. Lai et al. of NB-DOH [155] developed an HPLC procedure to assay meperidine and its degraded compounds.

Wilson et al. [156] determined fentanyl citrate by HPLC. The method was applied in stability studies and was applicable to the analysis of scale-up batches.

Menon et al. [157] has developed an HPLC procedure for analysis of sample solution of hydromorphone hydrochloride injection. However, it was only partially stability-indicating. Good separation of hydromorphone hydrochloride from morphine was observed, and identical HPLC conditions could be used to determine morphine in dosage forms.

Diamorphine and its hydrolysis products 6-acetylmorphine and morphine were determined simultaneously in aqueous solution by Barrett and Shaw [158]. HPLC was used to assess the stability of diamorphine (100 μ g/mL) in aqueous solution of pH 7.4 at 4°C, 25°C and 37°C.

XXXIII. *Parasympathomimetics*

Physostigmine sulfate and its degradation products in ophthalmic ointment was analyzed by Stewart and Quinn [159]. An accurate, precise and stability-indicating HPLC procedure was developed for the analysis.

The determination of chloramphenicol and its hydrolytic product in ophthalmic solutions was reported by Khalil et al. [160]. HPLC was applied to a stability study of commercial solutions of the drug stored at room temperature for up to 20 months.

Balansard et al. [161] developed a normal-phase HPLC for the determination of pilocarpine and isopilocarpine. This HPLC method was then applied to stability study of eye-drops based on pilocarpine. Good separation of pilocarpine and its degradation product isopilocarpine was achieved. The stability-indicating HPLC assay suggested that freeze-dried or acid-pH liquid eye-drops have low isopilocarpine levels (1% or less) compared with neutral-pH liquid eye-drops (>9%). Pilocarpine loss after 3 years at room temperature was 5% for freeze-dried eye-drops and 10% for liquid eye-drops.

XXXIV. *Preparations for Common Cold*

Hewala [162] described a stability-indicating HPLC assay for paracetamol, guaiphenesin, sodium benzoate, oxomemazine and their decomposition products, e. g. , 4-aminophenol and guaicol in cough syrup.

The determination of different cough-cold products was studied by Heidemann et al. [163] using three HPLC procedures. System (i) was used for phenylpropanolamine hydrochloride, pseudoephedrine hydrochloride, dextromethorphan hydrobromide, diphenhydramine hydrochloride, clemastine fumarate and chlorpheniramine maleate, system (ii) for paracetamol and system (iii) for guaiphenesin. Methods for extracting and analysing immediate-release and sustained-release tablets and granules are described.

Alvi and Castro [164] simultaneously separated acetaminophen [paracetamol] and hydrocodone tartrate in tablet formulations by a stability-indicating HPLC using a Radial Pak cartridge packed with ODS. Quantitation was by peak height and an external standard was used. Impurities and

degradation products, viz, p-chloroacetanilide and p-aminophenol, and other opiates, viz, hydromorphone hydrochloride and codeine sulfate, were separated from the two analytes. Another stability-indicating HPLC method for the simultaneous analysis of acetaminophen [paracetamol], codeine phosphate, sodium benzoate and their potential degradation products 4-aminophenol, codeine N-oxide and codeinone in elixirs was reported by Sisco et al. [165]. Sisco et al. [166] also developed a stability-indicating HPLC method for acetaminophen [paracetamol], codeine phosphate, and their potential degradation products 4-aminophenol, codeine N-oxide and codeinone in tablets and capsules.

XXXV. *Preservatives*

Bronopol lotion was analyzed, without pretreatment, by Lian et al. [167]. HPLC was applied in stability studies.

XXXVI. *Prostaglandins*

Prostaglandin E1 (PGE1), selected as a model prostaglandin and added to white petrolatum (WP), white ointment, hydrophilic petrolatum, and Plastibase, was extracted from the ointment and was determined by Yamamura and Yotsuyanagi [168] using HPLC. The described HPLC method was applied to the long-term stability stuides of PGE1 and its α -cyclodextrin complex incorporated into WP and macrogol ointment. Results indicated that the remaining PGE1 was high enough for therapeutically effective purposes.

Complete separation of enprostil from its degradation products was achieved by an HPLC procedure which was developed by Kenley et al. [169]. The effect, of the nature of stationary phase, composition of mobile phase and column temperature on the retention of enprostil were investigated.

Prostaglandins E2, A2 and B2 were simultaneously determined by Amin [170]. The HPLC method was employed for the stability studies of prostaglandin E2 in pharmaceutical preparations.

Carignan and Lodge [171] analyzed prostaglandin E2 [dinoprostone] raw material and tablets by an HPLC procedure. Separation of prostaglandin E2 , its isomers and its degradation products (prostaglandins A2 and B2) was achieved in 15 min.

XXXVII. *Radiopharmaceuticals*

Riley et al. [172] developed a selective and precise stability-indicating LC assay with UV detection. The preformulation characteristics of the radiosensitizer, 1,2,4-benzotriazin-3-amine 1,4-dioxide [benzo-1,2,4-triazin-3- amine-1,4-dioxide] (SR-4233, WIN-59075) in aqueous solution was described. Peak purity and characterization of degradation products was accomplished by multi-wavelength detection between 200 and 360 nm. The method was used to determine the aq. stability of WIN-59075 under a variety of accelerated conditions. The 3-month stability of various formulations of the drug at room temperature was also demonstrated in this work.

XXXVIII. *Sex Hormones*

Leroy et al. [173] determined oestradiol benzoate and its degradation products oestradiol and benzoic acid in an ointment by HPLC. The simultaneous determination of these drugs was successfully achieved in samples stored for ≦ 4 years.

XXXIX. *Sympathomimetics*

Bitolterol mesylate was separated from similar compounds by Wilson [174]. Stability studies showed no degradation over 12 months at 25°C, and 7% loss over 12 months at 40°C and this was confirmed by TLC.

Stability studies on salbutamol in buffer solution and investigation of its decomposition products were described by Malkki and Tammilehto [175] using an optimum HPLC method with diode-array detection.

Das-Gupta [176] used HPLC for the quantitation of terbutaline sulfate in pharmaceutical dosage forms. No interference was found from the various excipients present in the dosage forms. The method was stability-indicating as

shown by the presence of peaks from decomposition products.

Kirchhoefer et al. [177] analyzed USP epinephrine [adrenaline] injections for potency, impurities, degradation products and (+)-enantiomer by HPLC. Impurities at levels <1% were easily detected by their method.

XXXX. *Thyroid Agents*

Garnick et al. [178] developed an HPLC method with stability-indicating characteristics for sodium levothyroxine in dosage forms. The method can be also used in content uniformity studies of single tablets. No degradation or excipient interference was noted according to this paper.

Richheimer and Amer [179] reported a reverse phase high performance liquid chromatographic method for the determination of sodium levothyroxine in tablets. The studies of drug dissolution and tablet content uniformity were also illustrated.

XXXXI. *Vasodilators*

Wang et al. [180] studied the stability of nimodipine injection by HPLC. Impurities and excipients did not interfere. Results were compared with those by spectrophotometry.

Liu and Chen [181] studied the determination and stability of nifedipine injection by HPLC. Nifedipine was unstable in light but more stable to heat, and could be stored at room temperature for 3.6 years without decomposition. In addition, the analysis of nifedipine and related compounds in soft gelatin capsules was done by Bammi et al. [182]. Their method overcomes the deficiencies in the USP method due to its capability of separating the interfering component propylparaben. This procedure is recommended for regular in-check quality control release and evaluating both shelf-life stability of capsules and bulk drug.

Shivram et al. [183] determined diltiazem hydrochloride in tablets. Test determinations of decomposition products were carried out on hydrolysates obtained by 30-min. deacetylations under reflux at pH 5.5 or in 0.1M-HCl or 0.1M-NaOH. Diltiazem was completely separated from its decomposition products by HPLC. Diltiazem hydrochloride was also determined by Abdel-Hamid et al. [184]. It was reported that inter-assay coefficients of variation were 1.9, 3.1 and 0.5% for 2, 4 and 6 μ g/mL while intra-assay coefficients of variation were 2.0 and 2.4% for 4 and 6 μ g/mL, respectively. Several additives did not interfere.

A stability-indicating HPLC method for dipyridamole was developed by Bridle and Brimble [185]. To detect degradation products and to assess the precision and accuracy of an HPLC method for the assay and purity assessment of dipyridamole, the drug was investigated under various conditions, including refrigeration overnight. Results indicated that dipyridamole was well resolved from a synthetic by-product and degradation products. After refrigeration, a loss of up to 5% of drug was found. This method may be employed for stability and purity assays.

Renzi et al. [186] analyzed Bepridil hydrochloride in bulk form and in tablets, capsules and injection solution by HPLC. The method was suitable for determination of the drug, its degradation products and process impurities in both bulk drug and drug products.

The concentration of nitroglycerin in liquid dosage forms and IV admixture solutions was determined by Baaske et al. [187]. A coefficient of variation of less than 1.8% was achieved over a concentration range of 50-500 μ g/mL.

XXXXII. *Chinese Medicines*

Tsai and Chen[188] determined glycyrrhizin(GL), 18-α-glycyrrhetinic acid (18-α-GA) and 18-β-glycyrrhetinic acid (18-β-GA) in various extracts of licorice using HPLC with a photodiode-array detector. Detection was at 254 nm and excellent resolution was obtained. In another article, Tsai et al. [189] used an HPLC procedure to identify 18-α-GA and 18-β-GA in licorice which were heated at 37°C, 45°C or 55°C prior to analysis. 18-α-GA and 18-β-GA were found to be thermally stable on storage at 37°C to 55°C for 3 months.

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REFERENCES

97. Tenjarla, S. N. and Chow, D. S. L. 1993. Stability-indicating HPLC Assay of Propranolol for Transdermal Permeation Study. J. Liq. Chromatogr. 16 (13): 2899-2913.
98. Lee, Y. C.. Baaske, D. M. and Alam, A. S. 1984. High-performance Liquid-chromatographic Method for the Determination of Esmolol Hydrochloride. J. Pharm. Sci. 73 (11): 1660-1661.
99. Schroeder, A. C., DiGiovanni, J. H., Von-Bredow, J. and Heiffer, M. H. 1989. Pralidoxime Chloride Stability-indicating Assay and Analysis of Solution Samples Stored at Room Temperature for Ten Years. J. Pharm. Sci. 78 (2): 132-136.
100. Prue, D. G., Johnson, R. N. and Kho, B. T. 1983. High-performance Liquid-chromatographic Determination of Pralidoxime Chloride and Its Major Decomposition Products in Injectable Solutions. J. Pharm. Sci. 72 (7): 751-756.
101. Chi, H., Wang, Y. and Zhou, T. 1984. Liquid-chromatographic Assay of Gossypol Acetate Tablets and Stability Observation of Its Solutions. Yaowu Fenxi Zazhi 4 (6): 339-341.
102. Reif, V. D., Eickhoff, W. M., Jackman, J. K. and DeAngelis, N. J. 1987. Automated Stability-indicating High-performance Liquid-chromatographic Assay for Ethinyloestradiol and (levo)Norgestrel Tablets. Pharm. Res. 4 (1): 54-58.
103. Das-Gupta, V. 1983. Stability of Triamcinolone Acetonide Solutions as Determined by High-performance Liquid Chromatography. J. Pharm. Sci. 72 (12): 1453-1456.
104. Stoberski, P., Zakrzewski, Z. and Siedlecka, E. 1987. High-performance Liquid-chromatographic Studies on the Stability of Hydrocortisone Sodium Succinate in the Presence of Aminophylline in Some Infusion Fluids. Farm. Pol. 43 (7-8): 407-409.
105. Zakrzewski, Z. Stoberski, P. and Zdzieborska, M. 1990. Examination of Fenicort [Prednisolone Sodium Tetrahydrophthalate] Stability in Some Intravenous Solutions by HPLC. Farm. Pol. 46 (1-2): 19-22.
106. Bachman, W. J. and Gambertoglio, J. G. 1990. Implantable Infusion Pumps. Anal. Lett. 23 (5): 893-900.
107. Smith, E. W. and Haigh, J. M. 1989. In vitro Diffusion Cell Design and Validation. I. Stability-indicating High-performance Liquid-chromatographic Assay for Betamethasone Valerate in Purified Isopropyl Myristate Receptor Phase. Pharm. Res. 6 (5): 431-435.
108. Wanwimolruk, S. 1991. Rapid High-performance Liquid-chromatographic Analysis and Stability Study of Hydrocortisone 17-Butyrate in Cream Preparations. Pharm. Res. 8 (4): 547-549.
109. Melucci, C. K., Lyman, G. W., Bond, A. D. and Johnson, R. N. 1987. Determination of S-carboxymethylcysteine [carbocisteine] in Syrup Formulations by High-performance Liquid-chromatography. J. Chromatogr. 391 (1): 321-324.
110. Trivedi, R. J. 1988. Stability-indicating Liquid-chromatographic Determination of .alpha. Ionone in Toothpaste. J. Assoc. Off. Anal. Chem. 71 (1): 36-37.
111. Albert, K. 1985. Determination of Dithranol in Bulk and Pharmaceutical Formulations by HPLC. Pharm. Ztg. 130 (41): 2600-2604.
112. Pavelek, Z. and Benes, K. 1988.

Determination of Allantoin in Dosage Forms Containing a Complex of Iodine with polyvinylpyrrolidone. Cesk. Farm. 37 (1): 32-34.

113. Yamamoto, S., Ohtomo, M., Komatsu, K., Takamatsu, T. and Matsuoka, M. 1993. Stability of Allantoin and Identification of Its Degradation Compounds. Yakugaku Zasshi 113 (7): 515-524.
114. Trivedi, R. J. 1988. Stability-indicating Liquid-chromatographic Procedure for Determination of Allantoin in Cosmetic Lotion. J. Assoc. Off. Anal. Chem. 71 (2): 290-294.
115. Irwin, W. J., Li-Wan-Po, A. and Stephens, J. S. 1984. Noxythiolin: High-performance Liquid-chromatographic Assay and Stability. J. Clin. Hosp. Pharm. 9 (1): 41-51.
116. Mensink, C. K., Cox, H. L. M. and Van-de-Vaart, F. J. 1987. Stability and Quality of Tretinoin Raw Material. Pharm. Weekbl. 122 (19): 385-391.
117. Hitscherich, M. E., Rydberg, E. M., Tsilifonis, D. C. and Daly, R. E. 1987. Simultaneous Determination of Hydrochlorothiazide and Propranolol Hydrochloride in Tablets by High-performance Liquid Chromatography. J. Liq. Chromatogr. 10 (5): 1011-1021.
118. Frontini, R. and Mielck, J. B. 1992. Determination of Quantitation of Bendroflumethiazide [bendrofluazide] and Its Degradation Products Using HPLC. J. Liq. Chromatogr. 15 (14): 2519-2528.
119. Perlman, S., Szyper, M. and Kirschbaum, J. J. 1984. High-performance Liquid-chromatographic Analysis of Nadolol and Bendroflumethiazide [Bendrofluazide] Combination Tablet Formulations. J. Pharm. Sci. 73 (2): 259-261.
120. Stoberski, P., Zakrzewski, Z. and Szulc, A. 1988. Examination of Frusemide and Hydrocortisone Sodium Succinate Stability in Several Infusion Solutions by Reversed-Phase HPLC. Farm. Pol. 44 (7): 398-401.
121. Bauer, J., Quick, J., Krogh, S. and Shada, D. 1983. Stability-indicating Assay for Chlorthalidone Formulation: Evaluation of the USP Analysis and a High-performance Liquid-chromatographic Analysis. J. Pharm. Sci. 72 (8): 924-928.
122. Shen, Y. and Ye, M. Y. 1994. Determination of the Stability of Dopamine in Aqueous Solutions by High-performance Liquid Chromatography. J. Liq. Chromatogr. 17 (7): 1557-1565.
123. El-Sayed-Metwally, M. 1991. Stability-indicating High-performance Liquid-chromatographic Assay for .alpha. Methyldopa in Sustained-release Capsules. J. Chromatogr. 549 (1-2): 221-228.
124. Kafil, J. B. and Dhingra, B. S. 1994. Stability-indicating Method for the Determination of Levodopa, Levodopa-carbidopa and Related Impurities. J. Chromatogr. A, 667 (1-2): 175-181.
125. Tokunaga, H., Kimura, T. and Kawamura, J. 1984. Determination of Dihydroergotamine in Tablets by High-performance Liquid Chromatography and Stability in Aqueous Solution. Bunseki-Kagaku 33 (1): 26-30.
126. De-Schutter, J. A., De-Croo, F., Van-der-Weken, G., Van-den-Bossche, W. and De-Moerloose, P. 1985. Stability Study and Quantitative Determination of Mebeverine Hydrochloride in Tablets by Means of Reversed-phase High-performance Liquid-chromatography. Chromatographia 20 (3): 185-192.
127. Parasrampuria, J. and Das-Gupta, V. 1989. Quantitation of Famotidine in Pharmaceutical Dosage Forms Using High-performance Liquid-chromatography. Drug Dev. Ind. Pharm. 15 (12): 1989-1997.
128. Salem, M. A. S., Alkaysi, H. N. and Badwan, A. A. 1989. High-pressure Liquid-chromatographic Analysis and Dissolution of Famotidine in Tablet Formulation. Anal. Lett. 22 (11-12): 2501-2510.
129. Fatmi, A. A. and Williams, G. V., sen. 1989. Analysis of Metoclopramide and Related Compounds in Tablets by Liquid

Chromatography. Drug Dev. Ind. Pharm. 15 (9): 1365-1373.

130. Suleiman, M. S., Muti, H. Y., Abdel-Hamid, M. E., Hassan, M., El-Sayed, Y. M. and Najib, N. M. 1989. Stability-indicating HPLC Analysis of Famotidine and Its Application to Kinetic Studies. Anal. Lett. 22 (6): 1499-1512.
131. Suleiman, M. S., Najib, N. M., El-Sayed, Y. M. and Badwan, A. 1989. Stability-indicating High-performance Liquid-chromatographic Assay for the Determination of Metoclopramide Hydrochloride in Pharmaceutical Dosage Forms. Analyst (London) 114 (3): 365-368.
132. Hoyer, G. L., LeDoux, J. and Nolan, P. E., Jr. 1995. A Sensitive Stability Indicating Assay for the H_2 Blocker Ranitidine. J. Liq. Chromatogr. 18 (6): 1239-1249.
133. Bauer, J., Linton, C. and Norris, B. 1988. Stability-indicating High-performance Liquid-chromatographic Analysis of Tin Protoporphyrin and Other Free-acid Metalloporphyrins. J. Chromatogr. 445 (2): 429-432.
134. Buck, R. H., Cholewinski, M. and Maxl, F. 1991. Animal Test or Chromatography? Validated High-performance Liquid-chromatographic Assay as an Alternative to the Biological Assay for Ornipressin. J. Chromatogr. 548 (1 + 2): 335-341.
135. Subba-Rao, G. N., Sutherland, J. W. and Menon, G. N. 1987. High-performance Liquid-chromatographic Assay for Thyrotrophin-releasing Hormone and Benzyl Alcohol in Injectable Formulation. Pharm. Res. 4 (1): 38-41.
136. Wang, D. P. 1983. Stability of Procaine in Aqueous Systems. Analyst (London) 108 (1288): 851-856.
137. Torok, I., Fekete, J. and Paal, T. L. 1984. Stability-indicating Determination of Adrenaline in Injections Containing Procaine. J. Pharm. Biomed. Anal. 2 (3-4): 465-471.
138. Hu, O. Y. P., Chen, P. H., Fang, Y. J., Tang, H. S., Pao, L. H., Kwok, K. M. and King, M. L. 1992. Determination of Fenoverine, a Modulator of Smooth Muscle Motility, in Capsules and in Human Plasma: Application to Dosage Form Stability and a Pilot Study in Humans. J. Pharm. Sci. 81 (1): 91-93.
139. Paveenbampen, C., Lamontanaro, D., Moody, J., Zarembo, J. and Rehm, C. 1986. Liquid Chromatographic Determination of Folic Acid in Multivitamin Preparations. J. Pharm. Sci. 75(12): 1192-1194.
140. Kennedy, J. F., Rivera, Z. S., Lloyd, L. L., Warner, F. P. and White, C. A. 1989. Use of Reversed-phase HPLC for the Determination of Purity and Stability on Storage of L-ascorbic Acid Samples. J. Micronutr. Anal. 5 (4): 281-289.
141. Kmetec, V. 1992. Simultaneous Determination of Acetylsalicylic, Salicylic, Ascorbic and Dehydroascorbic Acid by HPLC. J. Pharm. Biomed. Anal. 10 (10-12): 1073-1076.
142. Caviglioli, G., Parodi, B., Cafaggi, S., Bignardi, G. and Romussi, G. 1994. Stability Indicating HPLC Assay for Retinoic Acid in Hard Gelatine Capsules Containing Lactose and as Bulk Drug Substance. Drug Dev. Ind. Pharm. 20 (15): 2395-2408.
143. Sisco, W. R., Schrader, P. A., McLaughlin, A. M. and Clark, B. H. 1986. Stability-indicating Reversed-phase High-performance Liquid-chromatographic Assay for Fenretinide in Soft Gelatin Capsules and Concentrated Corn Oil Suspensions. J. Chromatogr. 368 (1): 184-187.
144. Sisco, W. R. and DiFeo, T. J. 1985. Stability-indicating Reversed-phase High-performance Liquid-chromatographic Assay for Fenretinide [N-(4-hydroxyphenyl)retinamide] Drug Substance. J. Chromatogr. 322 (2): 380-385.
145. Hu, O. Y. P., Wang, S. Y., Fang, Y. J., Chen, Y. H. and King, M. L. 1990. Simultaneous Determination of Thiomersal and Chlorhexidine in Solutions for Soft Contact Lenses and Its Applications in Stability

Studies. J. Chromatogr. 523: 321-326.
146. Richard, A., Elbaz, M. and Andermann, G. 1984. Determination of 4-Chloroaniline and Chlorhexidine Digluconate by Ion-pair Reversed-phase High-performance Liquid Chromatography. J. Chromatogr. 298 (2): 356-359.
147. Unlu, N., Sumnu, M., Hincal, A. A. and Dalkara, S. 1987. Determination of Pilocarpine and Its Separation from Degradation Products by Reversed-phase High-pressure Liquid Chromatography in Ophthalmic Solutions. Hacettepe-Univ. Eczacilik-Fak. Derg. 7 (1): 1-13.
148. Bauer, J. and Krogh, S. 1983. High-performance Liquid-chromatographic Stability-indicating Assay for Naphazoline and Tetrahydrozoline in Ophthalmic Preparations. J. Pharm. Sci. 72 (11): 1347-1349.
149. Wall, G. M., Kenny, J. C., Fan, T. Y., Schafer, C., Ready, M. A., Baker, J. K., Ritter, P. and Scott, B. S. 1992. Analysis of 3- and 4-Monopivaloylepinephrine, Degradation Products in Dipivefrine Hydrochloride Drug Substance and Ophthalmic Formulations. J. Pharm. Biomed. Anal. 10 (6): 465-471.
150. Andermann, G. and Richard, A. 1984. Stability-indicating Determination of Tetrahydrozoline Hydrochloride in Ophthalmic Solutions by High-performance Liquid Chromatography. J. Chromatogr. 298 (1): 189-192.
151. Parhizkari, G., Miller, R. B. and Chen, C. 1995. A Stability-indicating HPLC Method for the Determination of Benzalkonium Chloride in Phenylephrine HCl 10% Ophthalmic Solution. J. Liq. Chromatogr. 18 (3): 553-563.
152. Bauer, J., Heathcote, D. and Krogh, S. 1986. High-performance Liquid-chromatographic, Stability Indicating Assay for Disodium EDTA in Ophthalmic Preparations. J. Chromatogr. 369 (2): 422-425.
153. Wu, S. C., Chen, F. S., Li, J. H., Liao, C. H. and Chen, G. L. 1993. A Stability-indicating Method for Morphine Assay by High-performance Liquid Chromatography. Chung-hua Yao Hsueh Tsa Chih 45 (2): 133-145.
154. Wu, S. C., Chen, F. S. and Li, J. H. 1995. Stability-indicating HPLC Method for the Determination of Morphine and Atropine in Morphine-atropine Injections. Chung-hua Yao Hsueh Tsa Chih 47 (5): 457-468.
155. Lai, C. J., Chen, F. S., Li, J. H., Liao, C. H. and Chen, G. L. 1993. The HPLC Stablity Indicating Method of Meperidine Hydrochloride. Chung-hua Yao Hsueh Tsa Chih 45 (2): 147-162.
156. Wilson, T. D., Maloney, T. and Amsden, W. B. 1988. High-performance Liquid-chromatographic Determination of Fentanyl Citrate in a Parenteral Dosage Form. J. Chromatogr. 445 (1): 299-304.
157. Menon, S. K., Burchett, M. K. and Joseph, J. C. 1989. High-performance Liquid-chromatographic Assay of Hydromorphone Hydrochloride Injection. J. Liq. Chromatogr. 12 (4): 657-671.
158. Barrett, D. A. and Shaw, P. N. 1994. A Stability Indicating HPLC Assay for Diamorphine in Aqueous Solution. J. Liq. Chromatogr. 17 (17): 3727-3733.
159. Stewart, J. T. and Quinn, K. D. 1989. High-performance Liquid-chromatographic Determination of Physostigmine and Its Degradation Products in Pharmaceutical Dosage Forms. J. Liq. Chromatogr. 12 (4): 673-683.
160. Khalil, S. A. H., Shah, A. H. and Al-Shareef, A. H. 1993. Reversed-phase HPLC Method for the Determination of Chloramphenicol and Its Hydrolytic Product in Ophthalmic Solutions. Anal. Lett. 26 (6): 1163-1179.
161. Balansard, G., Vidal, E., Guigues, M., Ollivier, B. and De-Meo, M. 1986. Determination of Pilocarpine and Isopilocarpine by Normal-phase High-performance Liquid Chromatography. Application to Stability Study of Eye-drops Based on Pilocarpine and Comparison of

This Method with a Colorimetric Method Involving Hydroxylamine. Pharm. Acta Helv. 61 (2): 47-50.

162. Hewala, I. I. 1994. Stability-indicating HPLC Assay for Paracetamol. Guaiphenesin, Sodium Benzoate and Oxomemazine in Cough Syrup. Anal. Lett. 27 (1): 71-93.
163. Heidemann, D. R., Groon, K. S. and Smith, J. M. 1987. HPLC Determination of Cough - cold Products. LC-GC 5 (5): 422-426.
164. Alvi, S. U. and Castro, F. 1987. Stability-indicating Simultaneous Analysis of Acetaminophen [paracetamol] and Hydrocodone Tartrate in Tablets Formulation by HPLC. J. Liq. Chromatogr. 10 (15): 3413-3426
165. Sisco, W. R., Rittenhouse, C. T., Everhart, L. A. and McLaughlin, A. M. 1986. Simultaneous high-performance Liquid-chromatographic Stability-indicating Analysis of Acetaminophen [paracetamol], Codeine Phosphate and Sodium Benzoate in Elixirs. J. Chromatogr. 354: 355-366.
166. Sisco, W. R., Rittenhouse, C. T. and Everhart, L. A. 1985. Simultaneous High-performance Liquid-chromatographic Stability-indicating Analysis of Acetaminophen [paracetamol] and Codeine Phosphate in Tablets and Capsules. J. Chromatogr. 348 (1): 253-263.
167. Lian, H., Zhang, W., Zhong, L., Li, L., Wu, X., Cheng, R. and Mao, L. 1989. Ion-pair Reversed-phase HPLC Determination of Bronopol and Its Stability. Yaowu Fenxi Zazhi 9 (4): 197-199.
168. Yamamura, K. and Yotsuyanagi, T. 1984. High-performance Liquid-chromatographic Assay for Prostaglandin E1 in Various Ointment Vehicles. Separation and Stability Testing. J. Chromatogr. 303 (1): 165-172.
169. Kenley, R., Lee, K. M., and Mahoney, T. R. 1986. Stability-specific HPLC Analysis of the Antiulcer Prostaglandin, Enprostil, in a Soft Elastic Gelatin Capsule Formulation. J. Liq. Chromatogr. 9 (16): 3577-3595.
170. Amin, M. 1989. Simultaneous Determination of Prostaglandins E2, A2 and B2 and Stability Studies of Prostaglandin E2 in Pharmaceutical Preparations by Ion-pair Reversed-phase HPLC. Pharm. Acta Helv. 64 (2): 45-50.
171. Carignan, G. and Lodge, B. A. 1985. Stability-indicating High-performance Liquid-chromatographic Procedure for the Analysis of Prostaglandin E2 [dinoprostone] Raw Material and Tablets. J. Liq. Chromatogr. 8 (8): 1431-1443.
172. Riley, C. M., Shetty, B. V., Chetwyn, N. C., Kasper, V. T., Kindberg, C. G. and Dicken, C. M. 1993. Stability-indicating Assay and the Preformulation Characteristics of the Radiosensitizer, 1,2,4-benzotriazin-3-amine 1,4-dioxide [benzo-1,2,4-triazin-3- amine-1,4-dioxide]. J. Pharm. Biomed. Anal. 11 (2): 131-138.
173. Leroy, P., Benoit, E. and Nicolas, A. 1986. Determination and Stability Study of Oestradiol Benzoate in a Pharmaceutical Ointment by High-performance Liquid Chromatography. J. Chromatogr. 367 (2): 428-433.
174. Wilson, T. D. 1987. High-performance Liquid-chromatographic Determination of Tornalate [bitolterol mesylate] in Solution Dosage Forms; a Specificity Study. J. Chromatogr. 391 (2): 409-418.
175. Malkki, L. and Tammilehto, S. 1993. Optimization of the Separation of Salbutamol and Its Decomposition Products by Liquid Chromatography with Diode-array Detection. J. Pharm. Biomed. Anal. 11 (1): 79-84.
176. Das-Gupta, V. 1986. Quantitation of Terbutaline Sulphate in Pharmaceutical Dosage Forms Using High-performance Liquid Chromatography. J. Liq. Chromatogr. 9 (5): 1065-1074.
177. Kirchhoefer, R. D., Sullivan, G. M. and Allgire, J. F. 1985. Analysis of USP Epinephrine [adrenaline] Injections for Potency, Impurities, Degradation Products

and (+)-Enantiomer by Liquid Chromatography, Using Ultra-violet and Electrochemical Detectors. J. Assoc. Off. Anal. Chem. 68 (2): 163-165.

178. Garnick, R. L., Burt, G. F., Long, D. A., Bastian, J. W. and Aldred, J. P. 1984. High-performance Liquid-chromatographic Assay for Thyroxine Sodium in Tablet Formulations: Content-uniformity Applications. J. Pharm. Sci. 73 (1): 75-77.
179. Richheimer, S. L. and Amer, T. M. 1983. Stability-indicating Assay, Dissolution, and Content Uniformity of Sodium Levothyroxine [thyroxine sodium] in Tablets. J. Pharm. Sci. 72 (11): 1349-1351.
180. Wang, S., Ma, W. and Wang, X. 1991. Studies on the Determination and Stability of Nimodipine Injection by HPLC. Yaowu Fenxi Zazhi 11 (2): 81-84.
181. Liu, C. Y. and Chen, G. R. 1993. Studies on the Determination and Stability of Nifedipine Injection by HPLC. Yaowu Fenxi Zazhi 13 (5): 314-317.
182. Bammi, R. K., Nayak, V. G., Bhate, V. R., Dhumal, S. N., Gaitonde, C. D. et al. 1991. Analysis of Nifedipine and Related Compounds in Soft Gelatin Capsules by Liquid Chromatography. Drug Dev. Ind. Pharm. 17(16): 2239-2244.
183. Shivram, K., Shah, A. C., Newalkar, B. L. and Kamath, B. V. 1992. Stability Indicating High-performance Liquid-chromatographic Method for the Assay of Diltiazem Hydrochloride in Tablets. J. Liq. Chromatogr. 15 (13): 2417-2422.
184. Abdel-Hamid, M. E., Suleiman, M. S., Najib, N. M. and Muti, H. 1988. Stability-indicating High-performance Liquid-chromatographic Determination of Diltiazem Hydrochloride. Anal. Lett. 21 (12): 2263-2275.
185. Bridle, J. H. and Brimble, M. T. 1993. Stability Indicating Method for Dipyridamole. Drug Dev. Ind. Pharm. 19 (3): 371-381.
186. Renzi, N. L., Fronheiser, M. E., Duong, H. T., Fulton, D. J. and Rabinowitz, M. 1989. Stability-indicating High-performance Liquid Chromatography Assay for Bepridil Hydrochloride Drug Substance and Drug Products. J. Chromatogr. 462: 398-405.
187. Baaske, D. M., Carter, J. E. and Amann, A. H. 1979. Rapid and Accurate Stability Indicating Assay for Nitroglycerin. J. Pharm. Sci. 68(4): 481-483.
188. Tsai, T. and Chen, C. F. 1991. Determination of Three Active Principles in Liquorice Extract by Reversed-phase High-performance Liquid Chromatography. J. Chromatogr. 542 (2): 521-525.
189. Tsai, T. H., Shen, C. C. and Chen, C. F. 1992. Determination and UV Spectral Identification of 18.alpha. Glycyrrhetinic Acid and 18.beta. Glycyrrhetinic Acid for Stability Studies. Int. J. Pharm. 84 (3): 279-281.

Table 1. Stability-indicating HPLC methods for drugs in pharmaceutical dosage forms (continued)

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
propanolol hydrochloride Ref. 97	in propylene glycol	CN column, 5 μm 15 cm×4.6 mm	aq. 47% acetonitrile containing 5mM-sodium heptane sulfonic acid, 1.9 ml/min	verapamil hydrochloride	230 nm
esmolol hydrochloride Ref. 98	bulk	μ-Bondapak CN, 10 μm, 30 cm×3.9 mm	acetonitrile - acetic acid - 0.068% Na acetate trihydrate buffer (15:1:84), 2 ml/min	methylpropanol	280 nm
pralidoxime chloride Ref. 99	solution	μ-Porasil, 10 μm 30 cm×3.9 mm	aq. 86% acetonitrile containing 8.36mM-tetra-ethylammonium chloride and 52.5mM-acetic acid, 1 or 1.5 ml/min		295 nm
pralidoxime chloride Ref. 100	injectable solutions	Spherisorb ODS, 5 μm 25 cm×3.2 mm	acetonitrile/aq. 5mM-H_3PO_4-1mM-tetraethyl-ammonium chloride (13:12), 0.8 ml/min		270 nm
gossypol acetate Ref. 101	tablets	Polyamid 6 D, 25 cm×5 mm	hexane - $CHCl_3$ - anhyd. acetic acid - cyclohexane (78:20:3:2), 2.1 ml/min		254 nm
ethinyloestra-diol norgestrel or levonorgestrel Ref. 102	tablets	C8 or C18 silica	H_2O - acetonitrile - methanol (9:7:3)		fluorimetry 310 nm (excitation at 210 nm), or 240 nm
triamcinolone acetonide Ref. 103	solutions	μ-Bondapak C18 30 cm×4 mm	0.02M-KH_2PO_4 containing 32% of acetonitrile (pH 4.2), 2.5 ml/min		254 nm
hydrocortisone sodium succinate and aminophylline Ref. 104	infusion fluids	LiChrosorb RP-18, 10 μm, 25 cm×4 mm	aq. 70% methanol, 1.2 ml/min		254 nm
Fenicort [prednisolone sodium tetra-hydrophthalate] Ref. 105	intravenous solutions	μ-Bondapak C18 30 cm×3.9 mm, stainless-steel	aq. 70% methanol, 0.84 ml/min		246 nm
prednisolone sodium phosphate Ref. 106	implantable infusion pumps	μ-Bondapak phenyl, 10 μm, 30 cm×3.9 mm	acetonitrile - 0.1M-NaH_2PO_4 buffer (1:3), 1.6 ml/min	phenacetin	243 nm
betamethasone valerate Ref. 107		ODS material	aq. 55% acetonitrile	norethisterone	
hydrocortisone 17-butyrate Ref. 108	cream	Nucleosil C18, 5 μm 15 cm×4.6 mm	acetonitrile - methanol - H_2O (1:11:8), 1 ml/min	hydrocortisone acetate	240 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
carbocisteine Ref. 109	syrup	Spherisorb NH_2, 5 μ m, 15 cm×4 mm stainless-steel	50mM-phosphate buffer - acetonitrile (3:1), 1 ml/min		220 nm
α -ionone, 4-hydroxy-benzoates Ref. 110	toothpaste	C18 material 30 cm×4.5 mm	0.01M-KH_2PO_4 - methanol - acetonitrile (9:7:4), 2 ml/min		230 nm or 265 nm
dithranol Ref. 111	bulk ointments	LiChrosorb RP-18	acetonitrile - H_2O - acetic acid (120:79:1),		394 nm
allantoin Ref. 112	pharmaceuticals	Separon SIX NH_2, 5 μ m, 15 cm×3.2 mm	aq. 70% acetonitrile, 0.5 ml/min		220 nm
allantoin Ref. 113		cation exchange MCI gel CK08S, 50 cm×8 mm	1% H_3PO_4, 1 ml/min		210 nm
allantoic acid and glyoxylic acid Ref. 113		anion exchange HPIC-A54, 25 cm×4 mm	3mM-sodium borate, 1.5 ml/min		conductometric detection
urea Ref. 113		YMC-Pak A312, 15 cm×6 mm	0.01M-SDS in H_3PO_4 of pH 2, 1 ml/min		200 nm
allantoin Ref. 114	cosmetic lotion	Zorbax NH_2, 10 μ m 25 cm×4.5 mm	aq. 0.1% triethylamine (pH 4.0) - acetonitrile (1:9), 2 ml/min		240 nm
noxythiolin Ref. 115		Hypersil-ODS, 5 μ m 10 cm×4.6 mm stainless-steel	H_2O, 1 ml/min		250 nm
tretinoin Ref. 116	raw material	LiChrosorb RP-18, 10 μ m, 25 cm×4.6 mm	methanol - H_2O - acetic acid (150:25:1), 1.8 ml/min		320 nm
hydrochloro-thiazid and propranolol hydrochloride Ref. 117	tablets	Ultrasphere Cyano, 5 μ m, 25 cm×4.6 mm	acetonitrile - 0.05M-$NH_4H_2PO_4$ (pH 3.0) (3:17), 2 ml/min		290 nm
bendroflume-thiazid Ref. 118		Nucleosil-100 Phenyl, 7 μ m, 300×4 mm; guard column: 5×4 mm; at 35°C	aq. 40% ethanol, 1.5 ml/min	salicylamide	250 nm
nadolol and bendroflume-thiazid Ref. 119	tablets	Waters Phenyl, 5- or 10- μ m, 25 to 30 cm×4.6 mm, at 32°C; saturator column preceded the injector: 37- μ m silica, 50 cm×2 mm	methanol - aq. acetate buffer (29mM-acetic acid, 10mM-Na acetate and 40mM-NaCl) (3:2), 1.5 to 2.5 ml/min		270 nm
frusemide, hydrocortisone sodium succinate Ref. 120	injections	LiChrosorb RP-18, 10 μ m, 25 cm×4 mm	aq. 70% methanol, 1.2 ml/min		254 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
chlorthalidone Ref. 121	pharmaceuticals	μ-Bondapak C18	acetonitrile - 2% acetic acid (3:7), 1.5 ml/min	4-nitroaniline	280 nm
dopamine Ref. 122	solutions	Biophase ODS, 5 μm, 10 cm×3 mm; guard column: C18/Corasil, 40 μm, 2 cm×4.5 mm	16.67mM-sodium phosphate/ 0.41mM-heptanesulfonic acid/80 μm -EDTA/3% methanol, 0.8 ml/min		amperometric detection
α-methyldopa Ref. 123	sustained-released capsules	Phenomenex CN, 5 μm, 25 cm×4.6 mm	aq. 20% methanol containing 2% of acetic acid and 5mM-Na heptane-1-sulphonate (pH 2.55 to 2.65), 1.6 ml/min		280 nm
levodopa, carbidopa Ref. 124	pharmaceuticals	μ-Bondapak C18, 10 μm, 25 cm×4.6 mm	0.05M-ammonium acetate with 1% methanol adjusted to pH 4.1 with 0.6M-acetic acid, 1 ml/min		280 nm followed by Coulochem detector screen electrode at +0.3 V and sample electrode at +0.6 V
dihydroergo-tamine mesylate Ref. 125	tablets	LiChrosorb RP-18 5 μm, 15 cm×4 mm at 35°C	acetonitrile - 0.1M-acetate buffer (pH 5) (9:11), containing 3mM-triethylamine, 1 ml/min	17-α-hydroxy-progesterone	260 nm
mebeverine hydrochloride Ref. 126	tablets	LiChrosorb RP-8, 10 μm	aq. 75% methanol containing 0.05% of hexylamine adjusted to pH 5.0 with H_3PO_4, 1 ml/min		263 nm
famotidine Ref. 127	tablets, suspensions, injection soln	μ-Bondapak C18 30 cm×3.9 mm	aq. 0.01M-KH_2PO_4 containing (by vol.) 12% of methanol, 2% of acetonitrile and 0.1% of anhyd. acetic acid, 2.0 to 3.6 ml/min	sulfamerazine	268 nm
famotidine Ref. 128	tablets	LiChrosorb RP-18, 7 μm, 25 cm×4.6 mm	0.01M-phosphate buffer - acetonitrile - methanol (84:11:5) adjusted to pH 6.5 with H_3PO_4, 1.8 ml/min	theophylline	280 nm
metoclopra-mide Ref. 129		C18	0.15M-ammonium acetate - acetonitrile (80:20)		268 nm
famotidine Ref. 130		Spherisorb ODS, 5 μm, 25 cm	ammonium acetate buffer (pH 2.9) - acetonitrile (21:4), 1.5 ml/min	salicylic acid	254 nm
metoclopra-mide hydrochloride Ref. 131	tablets	Spherisorb RP-C8, 5 μm, 25 cm×4.6 mm	phosphate buffer (pH 4.8) - methanol - acetonitrile (25:14:11), 1.5 ml/min	phenobarbitone	214 nm
ranitidine Ref. 132		Ultrasphere-ODS C18 25 cm×4.6 mm	acetonitrile/10mM-potassium phosphate buffer pH 5 (2:23), 2 ml/min	caffeine	262 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
tin protopor-phyrin and other metallo-porphyrins Ref. 133		PRP-1, 10 μ m 25 cm×4 mm	20mM-tetrabutylammonium hydroxide (pH 12) - acetonitrile (13:7) or 20mM-tetrabutylammonium hydroxide (pH 12) acetonitrile - methanol (2:5:3), 2 ml/min		400 nm
ornipressin Ref. 134		Hypersil ODS or Spheri 5, 5- μ m 12.5 or 10 cm× 4.6 mm; at 60°C or 80°C	linear gradient (10 to 60% over 25 min) of 0.02M-tetramethylammonium hydroxide (I) in aq. 50% acetonitrile added to aq. 0.02M-I, both adjusted to pH 2.5 with H_3PO_4, 1 ml/min		220 nm
protirelin (thyrotrophin-releasing hormone), benzyl alcohol Ref. 135	multidose injectable formulation	microparticulate ODS silica	aq. Na octanesulphonate (pH 2.2) - methanol - acetonitrile - triethyl-amine (92:4:4:0.01), 1.5 ml/min	4-aminobenzoic acid	215 nm
procaine Ref. 136	aqueous systems	μ -Bondapak C18 30 cm×4 mm, at 25°C to 28°C	methanol - aq. 1% acetic acid (2:3; pH 4.7), 1.1 ml/min		254 nm
adrenaline, procaine Ref. 137	injections	ODS-Sil-X-1, 30 cm×2.6 mm operated at 35°C	aq. 0.1mM-H_2SO_4 1 ml/min		205 nm
fenoverine Ref. 138	capsules	Nucleosil CN, 5- μ m; pre-column: Bondapak C18, at 45°C	acetonitrile - 0.1M-ammo-nium acetate (7:13), 1.5 ml/min	chlorpromazine	254 nm
folic acid Ref. 139	multivitamin preparations	μ -Bondapak C18 30 cm×3.9 mm; pre-column: 37 to 50 μ m Corasil C18 7 cm×2 mm	CH_3OH:CH_3CN:0.01 M NaOAc (6:4:90; pH 4.5, adjusted with HOAc), 2.5 ml/min		280 nm
ascorbic acid Ref. 140	bulk	PLRP-S, 5 μ m 15 cm×4.6 mm	0.2M-NaH_2PO_4 (pH 2.14, adjusted with HCl), 0.5 ml/min		220 and 268 nm
acetylsalicylic, salicylic, ascorbic and dehydroas-corbic acid Ref. 141	capsules	Nucleosil NH_2, 10 μ m 25 cm×4 mm 1.2 ml/min	acetonitrile - methanol - 0.02M-KH_2PO_4 buffer soln. of pH 3.5 (3:2:5),		280 nm or fluorimetric detection at 430 nm (excitation at 350 nm)
retinoic acid Ref. 142	capsules	LiChrospher 100 RP-18, 5 μ m, 25 cm×4 mm; guard column: 4×4 mm	acetonitrile/aq. 1% ammonium acetate (9:1), 1.25 ml/min		diode array detection at 340 nm (bandwidth 4 nm), reference wavelength at 500 nm (bandwidth 80 nm)
fenretinide Ref. 143	capsules, suspensions	Zorbax ODS, 5 μ m 25 cm×4.6 mm	acetonitrile - acidified H_2O, pH 3 (9:1), 2 ml/min		254 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
fenretinide Ref. 144		Zorbax ODS, 5 μ m 25 cm × 4.6 mm	acetonitrile - aq. acetic acid soln. at pH 2.0 (3:1), 2.0 ml/min		254 nm
chlorhexidine digluconate, 4-chloroaniline Ref. 145	ophthalmic preparations	μ -Bondapak C18, 10 μ m, 30 cm × 3.9 mm	acetate buffer soln. (pH 4.0) - acetic acid - methanol - Na heptane-sulphonate, 1.8 ml/min		
thiomersal, chlorhexidine gluconate Ref. 146		Nucleosil C18, 7 μ m	0.1M-KH_2PO_4 (pH 3.5) - methanol (2:3), 1.0 ml/min		254 nm
pilocarpine Ref. 147	ophthalmic solutions	Novapak C18, 5 μ m 30 cm × 4 mm	5% KH_2PO_4 soln. of pH 2 - methanol (193:7), 0.9 ml/min		215 nm
naphazoline, tetrahydrozo-line Ref. 148	ophthalmic solutions	μ -Bondapak C18	citrate buffer soln. (adjusted to pH 2.2 with $HClO_4$) - methanol (7:3), 2 ml/min		265 nm
dipivefrine hydrochloride Ref. 149	raw material opthalmic solns	μ -Bondapack, 5 μ m 30 cm × 3.9 mm	acetonitrile - 1% sodium dodecyl sulfate - anhyd. acetic acid (51:46:3), 2 ml/min		254 nm
tetrahydrozo-line hydrochlo-ride Ref. 150	ophthalmic solns	μ -Bondapak C18, 10 μ m, 30 cm × 3.9 mm	$Na_2B_4O_7$ - KH_2PO_4 buffer soln. of pH 7.0 - acetonitrile (3:2)		254 nm
benzalkonium chloride, phenylephrine hydrochloride Ref. 151	ophthalmic solutions	μ -Bondapak, 10 μ m 30 cm × 3.9 mm stainless-steel	50mM-potassium phosphate/ 57mM-sodium hexane sulfonate buffer of pH 6.3 containing 65% acetonitrile, 1.8 ml/min		215 nm
disodium EDTA Ref. 152	ophthalmic solutions	μ -Bondapak C18 30 cm × 4 mm	1M-tetrabutylammonium hydroxide - H_2O (adjusted to pH 7.5 with H_3PO_4) - methanol (1:91:8)	disodium nitrilotriacetate	254 nm
morphine, morphine HCl, morphine sulphate Ref. 153	solutions	Nucleosil C18 10 μ m, 30 cm × 4 mm	methanol/aqueous solution (containing 1% ammonium acetate, 1% acetic acid, 0.8% triethylamine and 0.017% sodium 1-heptane-sulfonate) = 15:85, 1.0 ml/min		284 nm using a photodiode-array detector
atropine sulphate Ref. 154	injections	Nucleosil C18 10 μ m, 30 cm × 4 mm	methanol/aqueous solution (containing 1% ammonium acetate, 1% acetic acid, 0.8% triethylamine and 0.017% sodium 1-heptane-sulfonate) = 30:70, 1.0 ml/min		258 nm using a photodiode-array detector
meperidine hydrochloride Ref. 155	aqueous solutions	Nucleosil C18 10 μ m, 30 cm × 4 mm	25% acetonitrile and 75% aqueous soln. (containing 0.5% H_3PO_4 and 0.7% triethylamine), 1.0 ml/min	phenol	254 nm using a photodiode-array detector

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
fentanyl citrate Ref. 156	parenteral dosage form	Partisil ODS-3, 10 μ m 25 cm×4.6 mm	H_2O - methanol - 85% H_3PO_4 (125:125:1), 1.0 ml/min		229 nm
hydromorphone hydrochloride, morphine Ref. 157		Nucleosil C18, 5 μ m 15 cm×4.6 mm	aq. 40% acetonitrile containing 1% of anhyd. acetic acid and 0.5% of Na dodecyl sulphate, 1.5 ml/min		280 nm
diamorphine, morphine, 6-acetylmorphine Ref. 158	aq. solution	Hypersil BDS C18, 5 μ m, 15 cm×4.6 mm	0.05M-K_2HPO_4 of pH 3/ acetonitrile (4:1), 1 ml/min		
physostigmine sulphate Ref. 159	ophthalmic ointment	Brownlee ODS, 5 μ m 10 cm×4.6 mm	acetonitrile - 0.6% Na dodecyl sulphate soln. in 0.05M-NaH_2PO_4 of pH 4.0 (2:3), 1.0 ml/min	procaine hydrochloride	310 nm
chloramphenicol Ref. 160	ophthalmic solutions	μ -Bondapak C-18 5 μ m, 30 cm×3.9 mm	H_2O/methanol/NH_3 (29:20:1, pH 7 adjusted with acetic acid, 1.5 ml/min		278 nm
pilocarpine, isopilocarpine Ref. 161	liquid eye-drops	Waters spherical silica, 5 μ m	hexane - propan-2-ol containing aq. 2% NH_3 (3:1)		220 nm
paracetamol, Guaiphenesin, sodium benzoate Ref. 162	cough syrup	C18 material, 5 μ m 25 cm×4.6 mm; guard column: 5 cm×4.6 mm	aq. 18% methanol at pH 3.9 for 12 min followed by aq. 80% methanol at the same pH for 10 min, 1.5 ml/min	metronidazole	235 nm
oxomemazine Ref. 162	cough syrup	C18 material, 5 μ m 25 cm×4.6 mm; guard column: 5 cm×4.6 mm	aq. 40% methanol containing 0.05% heptanesulfonic acid adjusted to pH 3	salbutamol sulfate	
phenylpropanolamin hydrochloride, pseudoephedrine hydrochloride, dextromethorphan hydrobromide, diphenhydramine hydrochloride, clemastine fumarate and chlorpheniramine maleate Ref. 163	tablets, granules	Zorbax 300-SCX cation exchanger 15 cm×4.6 mm	acetonitrile - ethylenediamine sulphate buffer soln. of pH 4.52 (7:13), 2 ml/min		216.5 nm
paracetamol Ref. 163	tablets, granules	Spheri-5 C18, 5 μ m 3 cm×2.1 mm	citrate buffer soln. of pH 6.0, 1 ml/min		250 nm
guaiphenesin Ref. 163	tablets, granule	Spheri-5	acetonitrile - citrate buffer soln. of pH 6.0 (3:37), 1 ml/min		230 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
acetaminophen, hydrocodone tartrate Ref. 164	tablets	ODS, 4 μ m 10 cm×4.8 mm Radial Pak cartridge	0.02M-K_2HPO_4 (containing 0.02% of triethylamine and 0.02% of H_3PO_4, adjusted to pH 3.3) - acetonitrile (21:4)		215 nm
acetaminophen, codeine phosphate, sodium benzoate Ref. 165	elixirs	μ -Bondapak C18, 30 cm×3.9 mm at 50°C	buffer soln. (15mM-Na butane-1-sulphonate - 15mM-KH_2PO_4 containing 2 ml/l of triethylamine, pH 4.8) - methanol (4:1), 2 ml/min		214 nm
acetaminophen, codeine phosphate Ref. 166	tablets capsules	μ -Bondapak C18, 30 cm×3.9 mm, at 40°C	15mM-potassium phosphate - triethylamine buffer (pH 2.35) - methanol (93:7), 3.0 ml/min		214 nm
bronopol Ref. 167	lotion	Micropak MCH-5 ODS, 5 μ m, 15 cm×4 mm	methanol - aq. 0.5% PICB-5 ion-pair reagent (11:89), 1 ml/min		254 nm
prostaglandin E1 Ref. 168	ointment	μ -Bondapak C18, 10 μ m, 30 cm×3.9 mm	0.02M-KH_2PO_4 (pH 4.9) - acetonitrile (3:2)		214 nm
enprostil Ref. 169	capsules	Partisil 5 ODS-3 10 cm×4.6 mm, at 40°C	THF - methanol - 1mM-phosphate buffer of pH 6.5 (3:6:11), 1 ml/min		220 nm
prostaglandin E2, A2, and B2 Ref. 170	pharmaceuticals	LiChrosorb RP-18, 5 μ m, 12 cm×4 mm	methanol - H_2O (11:9) containing octane-1-sulphonic acid or (36:29) containing tetrabutylammonium perchlorate, 2 ml/min		208, 228 and 298 nm for prostaglandins E2, A2 and B2
prostaglandin E2, A2, and B2 Ref. 170	pharmaceuticals	μ -Bondapak C18, 10 μ m, 10 cm×4.8 mm stainless-steel	methanol - butanol - acetic aid - H_2O (70:9:1:80)		208, 228 and 298 nm for prostaglandins E2, A2 and B2
prostaglandin E2 Ref. 171	raw material, tablets	Ultrasphere-CN, 5 μ m, 25 cm×4.6 mm	$CHCl_3$ - hexane (7:3)	testosterone	254 nm
benzo-1,2,4-triazin-3-amine-1,4 dioxide Ref. 172	aqueous solution	ODS Hypersil, 5 μ m 15 cm×4.6 mm	acetonitrile - 0.1M-phosphate buffer (pH 7) - triethylamine (230:20:1), 1.5 ml/min		diode array detector at 265 nm
oestradiol benzoate Ref. 173	ointment	LiChrosorb RP-18, 7 μ m, 25 cm×4 mm; pre-column: 3 cm×4 mm LiChrosorb RP-18, 40 μ	methanol - H_2O (9:1), 1.5 ml/min		230 nm
oestradiol Ref. 173	ointment	LiChrosorb RP-18, 7 μ m, 25 cm×4 mm; pre-column: 3 cm×4 mm LiChrosorb RP-18, 40 μ	methanol - H_2O - HOAc (60:35:5), 1.2 ml/min		E = +0.85 V vs. S.C.E.
benzoic acid Ref. 173	ointment	LiChrosorb RP-18, 7 μ m, 25 cm×4 mm; pre-column: 3 cm×4 mm LiChrosorb RP-18, 40 μ	methanol - H_2O (8:2), 1.0 ml/min	cyclohexane carboxylic acid	328 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
tornalate [bitolterol mesylate] Ref. 174		Partisil ODS-3 (10 μ m) ODS-3 (5 μ m), IBM (5 μ m) and Brownlee RP-18 (5 μ m), 25 cm×4.6 mm	H_2O - acetonitrile - acetic acid (19:30:1) containing 0.065% of Na octanesulphonate		254 nm
salbutamol Ref. 175		LiChrosorb RP-18	aetonitrile - 40mM-sodium dihydrogen phosphate - 6.74mM-triethylamine (pH 3.0); acetonitrile was increased from 4% to 9% after 6 min		diode-array detection
terbutaline sulphate Ref. 176	aerosols, injections, tablets	μ -Bondapak Phenyl 30 cm×3.9 mm	8% methanol in 0.02M-KH_2PO_4 (pH 3.6), 2 ml/min	salicylic acid	278 nm or 330 nm
epinephrine [adrenaline] Ref. 177	injections	Zorbax CN 25 cm×4.6 mm	aq. soln. containing 5mM-Na octanesulphonic acid, 0.1mM-Na_2EDTA, 2% acetonitrile and 1% methanol, adjusted to pH 3.5 with anhyd. acetic acid, 1.5 ml/min		254 nm
(+)-adrenaline Ref. 177	injections	Hibar column of LiChrosorb RP-18	methanol - phosphate buffer of pH 2.92 (13:27), 2 ml/min		254 nm
thyroxine sodium Ref. 178	tablets	Zorbax-CN	aq. 40% acetonitrile containing 0.05% of H_3PO_4		225 nm
thyroxine sodium Ref. 179	tablets	μ -Bondapak C18 30 cm×4 mm	60% of acetonitrile in aq. buffer soln. (pH 3.0; containing 5mM-octane-1-sulphonic acid and 5mM-tetramethylammonium chloride)		230 nm
nimodipine Ref. 180	injections	YWG $C_{18}H_{37}$ 25 cm×4 mm stainless steel	methanol - H_2O - ethyl ether (35:15:4), 1 ml/min	beclomethasone dipropionate	238 nm
nifedipine Ref. 181	injections	Zorbax-ODS 15 cm×4.6 mm at 40°C	aq. 65% methanol, 1.1 ml/min	thymol	235 nm
nifedipine Ref. 182	capsules		methanol-water (55:45)		265 nm
diltiazem hydrochloride Ref. 183	tablets	Rexchrome ODS 25 cm×4.6 mm	0.05M-KH_2PO_4 - aceto-nitrile- methanol (11:5:4), 2.0 ml/min	cyproheptadine hydrochloride	240 nm
diltiazem hydrochloride Ref. 184	bulk	Micropak MCH-5 15 cm×4 mm	aq. 48% acetonitrile (pH 3.3) containing 0.01M-Na octanesulphonate, 1 ml/min	clonazepam	239 nm

Table 1. Continued

Drugs	Materials	Columns	Mobile phases	Internal standards	Detection
dipyridamole Ref. 185		Phenomenex ODS 1, 5 μ m, at 60°C, 25 cm×4.6 mm	methanol - aq. 200mM-sodium pentane sulfonate (7:3) containing triethylamine (2 ml/l), adjusted to pH 3 with phosphoric acid, 1.5 ml/min		288 nm
bepridil hydrochloride Ref. 186	bulk, tablets, capsules injection soln.	μ -Bondapak C18, 10 μ m, 30 cm×4.6 mm, at 35°C	acetonitrile - Na heptane -1-sulphonate adjusted to pH 2.37 with acetic acid (116:81), 1.3 ml/min		254 nm
nitroglycerin Ref. 187	solutions IV admixtures	μ -alkyl phenyl, 10 μ m, 30 cm×3.9 mm	acetonitrile - tetrahydrofuran - water (26:10:64), 2 ml/min		218 nm
glycyrrhizin, 18- α -GA, 18- β -GA Ref. 188	liquorice	LiChrospher 100 RP-18, 5 μ m, 12.5 cm×4 mm; guard column: 4 mm ×4 mm	gradient of methanol - perchlorate buffer (pH 7.5 to 7.7), 1 ml/min		254 nm using a photodiode-array detector
18- α -GA, 18- β -GA Ref. 189	liquorice	LiChrospher RP-18 12.5 cm×4 mm; guard column: 4×4 mm	methanol - H_2O - NH_3 soln. - $HClO_4$ (200:50:1:1; pH 7.5), 1 ml/min)		254 nm or with photo-diode array detection from 200 to 380 nm

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安定性指標之高效液相層析法

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摘　要

本文綜合論述用以分析各類製劑中藥物成分之安定性指標高效液相層析法。文中與藥物安定性研究有關之文獻共一百八十九篇。由於藥物種類非常的多，因此，依據藥物之藥理作用予以分類。本文附有包含藥物名稱、藥物劑型、層析管類別(含流速)、移動相組成、內部標準品及偵測方式之簡表，以幫助讀者為工作需要而選取有參考價值的分析方法。

關鍵詞：藥物安定性，安定性指標，高效液相層析法。