Abstract

A program NABTIT written in BASIC has been developed for the treatment of data (ml/mV) obtained from potentiometric acid—base titrations in non-aqueous solvents. No preliminary information on equilibrium constants is required for the input. The treatment of the data is based on known equations and uses least-squares procedures. The essence of the method is to determine the equivalence volume \( V_e \) accurately, and to use the data acquired by adding titrant after \( V_e \) for the pH*-calibration of the non-aqueous potentiometric cell. As a by-product of the calculations, the pK* value of the substance titrated is also obtained, and in some cases the autoprotolysis constant of the medium (pK*\_s). Good agreement between experiment and theory was found in the treatment of data obtained for water and methanol—water mixtures.

Цитати:

3. José Barbosa, Dolores Barrón, JoséLuis Beltrán, Victoria Sanz-Nebot, PKPOT, a program for the potentiometric study of ionic equilibria in aqueous and non-aqueous media, Analytica Chimica Acta, 317, 1-3, 75-81, 1995,
6. Saeeduddin, Khanzada, A.W.K., Mufti, A.T. Dissociation constant studies of citric acid at different temperatures and in different organic-water solvent systems, Journal of Chemical Society of Pakistan 18, 2, 81-87, 1996. I.F. 0.221


12. Indhar, H.A.B., Khanzada, A.W.K., Potentiometric determination of dissociation constants and gibb’s free energies of 8-hydroxyquinoline (oxine) and 2-methyluinoiline using aqueous and mixed organic-water solvent systems, *Journal of the Chemical Society of Pakistan* **24**, 1, 3-9, 2002. I.F. 0.081


Abstract

Galanthamine hydrobromide (Nivalin®, dose 10 mg) was given subcutaneously and orally to 8 volunteers. Galanthamine and its metabolites were quantified in plasma and urine by reversed-phase HPLC. An unusual two-stage absorption and biexponential drug decline were observed. Galanthamine plasma peaks (1.24 μg/ml after subcutaneous and 1.15 μg/ml after oral doses) were reached 2 h following administration, the $t_{1/2}(β)$ values being 5.70 and 5.26 h, respectively. Minor epigalanthamine and galanthaminone plasma levels were detected. An almost complete urinary recovery of galanthamine and its metabolites was obtained within 72 h. The plasma AUC, $C_{max}$, $t_{max}$ and $k_{a}$ suggest that the subcutaneous and oral Nivalin formulations are bioequivalent.

Цитати:


I.F. 1.020

I.F. 1.333

I.F. 2.989

34. F Huang, KC Lasseter, L Janssens, T Verhaeghe, H Lau, Q Zhao, Pharmacokinetic and safety assessments of galantamine and risperidone after the two drugs are administered alone and together, *J. Clin. Pharmacol.*, 42, 12, 1341-1351, 2002.  
I.F. 2.167

I.F. 2.167

I.F. 4.204

I.F. 1.104

I.F. 1.269

I.F. 1.104

I.F. 0.642

I.F.0.422

I.F.1.243

I.F. 3.899


I.F. 1.420


I.F. 2.163

I.F. 2.167


Abstract

The influence of a new surfactant Linopharm on Vitamin A and vitamin E absorption is studied after oral administration on rats. The biopharmaceutical parameters are calculated by means of plasma levels data, determined by high-performance liquid chromatographic method. The results obtained show that the intestinal absorption of the solubilized Linopharm form is greater than that of the oil solutions and almost equal to this of Cremophor EL solubilize.

4. Ж. Тенчева, М. Колева, Ст. Михайлова, В. Бакалов, Течно-хроматографски методи за количествено определяне на витамините В₁, В₂, В₆ и РР в препарата „В-комплекс“-таблетки, сироп и инжекционен разтвор, Фармация, 1990.

Abstract

Liquid chromatography methods were developed for assaying the vitamins B₁, B₂, B₆, PP and antypirine in the dosage forms B-complex-tablets, syrup and injection solution. The separation was carried out in chromatography column Hibar-Lichrosorb RP 18, 5 μm (125 x 4 mm). Eluents with the following composition were used:

a) Distilled water, containing 10⁻⁹ M tetraethylammonium bromide (TEAB) and 1 per cent acetic acid (for separation and determination of the vitamins B₁, B₂, B₆ and PP in B-complex-tablets).

b) Distilled water, containing 10⁻⁹ TEAB and 0.25% acetic acid (for separation and determination of the vitamins B₁, B₂, B₆ and PP in B-complex-syrup and injection solution).

c) Mixture of methanol and water in ratio 30:70% (v/v), containing 10⁻³ M TEAB and 1% acetic acid (for assaying of Vitamin B₂ in three pharmaceutical dosage forms and of antipyrine in the injection solution). The methods are reproducible, quick and easy to perform.

Цитати:

1. Шелеметьева, Ольга Владимировна, Определение витаминов методом высокоэффективной жидкостной хроматографии в премиксах, биологически активных добавках и пищевых продуктах, Диссертация, Томск, 2009.

5. Ж. Тенчева, В. Бакалов, М. Колева, Ст. Михайлова, Количествено определяне на йохимбинов хидрохлорид и на витамините PP и E в препарата Тонисекс-капсули с помощта на ВЕТХ, Фармация, XLI (5-6), 6-10, 1991.

Abstract

A HPLC method for quantitative determination of yohimbine hydrochloride and vitamins PP and E in Tonisex-capsules is developed. The separation of the components is made by means of a column with reverse phases RP-18, 7 μm (250 x 4 mm). The suitable mobile phase, chosen experimentally, proved to be methanol/water mixture (99:1 v/v) with addition of 2.10⁻⁴ M DBA. The pH of the phase is 7. The
The extraction of the determined components from the drug form is realized by means of mixed solvent isopropanol/chloroform (2:1). The evaluation of the proposed method based on the analysis of 6 samples show that its reproducibility is very good. The method is fast and easy for realization, suitable for routine analysis.


Abstract

There were conducted preliminary investigations for the influence of some commonly used in the tablet production additives on the solubility and stability of nitrendipin. For the purpose were prepared physical mixtures and solid dispersions with additives, possessing expressed hydrophilic properties by the solvent method. From the group of surface active agents was investigated the influence of Tween 80 and sodium laurilsulphate on the solubility of nitrendipin in concentrations admissible for usage in solid dosage forms. With the most perspective in respect of the solubility additives were developed tablet models. There were used different approaches for incorporating of the drug substance. On the basis of the obtained profiles of dissolution comparatively with the commercial preparation Byotensin (Bayer) were selected additives and technological approach for development of tablet form.


Abstract

The elemental composition of seven soils of the main geographical regions in Bulgaria for the growth of Leucojum aestivum L. was determined. It was found that a relationship exists between the galanthamine content of the plant and the chemical composition of the soil. These results indicate that galanthamine biosynthesis could be controlled by the soil fertility level. indicate that galanthamine biosynthesis could be controlled by the soil fertility level.

Цитати:
Abstract

Metamizol (dipyrone) is hydrolyzed in gastrointestinal tract to the pharmacologically active metabolite 4-methyl-amino-antipyrine (4-MAA), which is transformed by both, oxidation to 4-formyl-amino-antipyrine (4-FAA) and demethylation to 4-amino-antipyrine (4-AA). 4-AA is acetylated to 4-acetyl-amino-antipyrine (4-AcAA). The aim of the present study was to investigate whether cimetidine will alter the pharmacokinetics of the metabolites of metamizol due to cimetidine-induced inhibition of the metabolic transformation of 4-MAA. The study was carried out in 12 patients with duodenal ulcer treated with cimetidine 1,000 mg daily over 20 days. A single oral dose of metamizol 1,500 mg was administered 2 days prior to commencement of cimetidine therapy to all patients. Two further doses of 750 and 1,500 mg of metamizol were given in a randomized order on days 8 and 13 during cimetidine treatment. Blood samples for determination of metamizol metabolites were drawn over 48 hours post dose. Drug assays for metamizol metabolites and cimetidine were performed using HPLC methods. The patients were phenotyped for CYP2D6 and acetylation polymorphism. The results revealed that cimetidine interacted with 4-MAA by increasing the systemic clearance of 4-MAA, whereas the renal clearance of 4-MAA remained unchanged. Consistent with cimetidine-induced changes in the oxidation of 4-MAA to 4-FAA, as well as the demethylation of 4-MAA to 4-AA, were the decreased rates of production and the lower maximum concentrations of 4-FAA and 4-AA when metamizol was administered during cimetidine treatment (p<0.05). No correlation was found between the decrease in the production rates of 4-FAA induced by cimetidine and the hydroxylation abilities of the patients, this suggesting that CYP2D6 is not involved in the metabolism of 4-MAA to 4-FAA. The acetylation of 4-AA to 4-AcAA was not affected by cimetidine. Cimetidine produced an increase not proportional to the dose in the systemic availability only of 4-MAA, whereas the kinetics of the other metabolites changed proportionally to the increasing dose of metamizol.

ЦИТАТИ:


Abstract

The bioavailability of 4-methyl-amino-antipyrine (4-MAA) and 4-amino-antipyrine (4-AA), the two pharmacologically active metabolites of metamizol, was compared after administration of a test (Analgin®, tablets, Sopharma, Bulgaria) and a reference formulation (Novalgin®, Hoechst, Germany) at single oral doses of 1 g metamizol. The study was conducted in 18 healthy volunteers according to a randomized, cross-over, with a 7 day-interval between the two medications. The results revealed that the plasma concentrations/time profiles for 4-MAA and 4-AA were similar after the administration of test (T) and reference ® formulations. For 4-MAA, the intra individual ratios T/R with 90%-confidence intervals of the area under the plasma concentrations/time curves (AUC), as well as the maximum plasma concentrations (Cmax) amounted to 0.95 (0.87-1.03) mg.h/ml and 0.96 (0.92-1.0) μg/ml, respectively. The two parameters were within the bioequivalence ranges. For 4-AA, the intra individual ratios T/R of AUC and Cmax were 0.99 (0.9-1.06) mg.h/ml and 1.01 (0.94-1.08) μg/ml, respectively, and laid within the bioequivalence ranges. The time for achieving Cmax in plasma for both metabolites did not differ significantly between test and reference formulation. Previous investigation indicated that Analgin (Dupnitza), the other oral metamizol formulation marketed in the country, was bioequivalent to Novalgin. Thus “different bioavailability” of the formulations, produce of Bulgaria, can be disregarded as a factor explaining the low risks of metamizol induced agranulocytosis in Bulgaria.


Abstract

The new curriculum of five years studies in the Faculty of Pharmacy in Sofia is presented. It comprises about 4000 hours which are obligatory to attend. After two years of studies a student can choose one of two fields of majoring: practical pharmacy and industrial pharmacy. The degree of Master of Pharmacy is conferred after graduation which can either with the state examinations or by preparation and defense of the diploma thesis.

Abstract
Comparative toxicological and pharmacological trials with widely used for treatment of manic disorders Li carbonate and Li-DL-aspartate were carried out. The results indicate that Li-DL-aspartate has weaker toxicity and better antidepressive effect in doses 1/10 to 1/40 DI50. The main physicochemical and in vitro biopharmaceutical characteristics Li-DL-aspartate synthesized in Department of Organic Chemistry, Higher Institute of Chemical Technology, Sofia, were determined. The stability of the substance in solid state and in 0.1 M NaOH and 0.1M HCl were investigated.


Abstract
A thin layer chromatography (TLC) densitometric method was developed for quantification of mangiferin (M) and isomangiferin (IM), the natural xanthone C-glucoside isomers. A mobile phase of ethyl acetate-formic acid-water (67:13:20) and cellulose plates were used for the separation of the two compounds. For 150 - 350 ng of analyte, the relative standard deviation was 2 - 6 % (n = 6) for both analytes. The compounds were determined in leaves of Cratoxylum pruniflorum Kurz. (0.23 % for M and 0.07 % for IM) and in the herb of Hypericum aucheri Jaub. et Spach (0.21 % for M and 0.03 % for IM).

Цитати:

Abstract
The activation of prodrugs in the body is maintained mainly by enzymatic hydrolysis. In the present review, the possible mechanisms of hydrolysis, as well as some structural effects on the hydrolysis rate are observed in detail. The possibilities for control of the hydrolytic cleaving of the ester bond and design of esters as prodrugs with desired stability are discussed. The trends for utilization of the prodrug approach and the recent achievements in its development are summarized.


Abstract
7-Theophyllinylacetoxglycols may be regarded as potential prodrugs. The model stability of four of these esters was investigated by means of their hydrolysis product (7-theophyllineacetic acid), produced in aqueous medium at different pH-values (1.2, 7.4 and 9.0). For separation of both substances and analysis of the acid, a rapid, simple and sensitive HPLC method was developed. The chromatographic procedure was validated and showed good accuracy and precision. The results showed that the synthesized esters were quite resistant to chemical hydrolysis under described conditions.


Abstract
A number of esters which derived from 7-theophyllineacetic acid were prepared. The stability of 7-theophyllinylacetoxglycols was evaluated in sodium hydroxide solution (pH 13.0) at 60°C. The degradation reaction was monitored by using a HPLC assay with ultraviolet detection. All of esters were hydrolyzed to yield the correspondence quantitative amount of the hydrolytic product. The rate constants of the hydrolytic decomposition of the described esters were estimated. The chemical mediated conversion displayed first-order kinetics, and half-lives of hydrolysis were determined too. Also, the availability of the esters to release 7-theophyllineacetic acid through diluted human plasma at 37°C was studied. Compounds were found to possess a high stability at these conditions. It was noticed that no spontaneous hydrolysis of ester derivatives was noticed within 24 hr as revealed by HPLC analysis. The aqueous solubility and lipophilicity (expressed as log P) of 7-theophyllineacetic acid and its esters were investigated by means of UV-spectrophotometry. It was found that all of the esters were more lipophilic than its patent molecule. However, their solubility in aqueous media was described, compared by the parent drug.
Based on precise analysis of the acid-base equilibrium, a new approach in the treatment of experimental data from a potentiometric titration is proposed. A new general formula giving explicitly the relation $V = f([H^+])$ is derived, valid for every acid-base titration, which includes mono- and polyfunctional protolytes and their mixtures. The present study is the first practical application of this formula for the simplest case, the analysis of one monofunctional protolyte. The collected mV data during the titration are converted into pH-values by means of an auto pH-calibration procedure, thus avoiding preliminary preparation of the measuring system. The mentioned pH-calibration method is applicable also in water-organic mixtures and allows the quantitative determination of sparingly soluble substances (particularly pharmaceuticals). The treatment of the data is performed by means of ready-to-use software products, which makes the proposed approach accessible for a wide range of applications.

**Цитати:**


**Abstract**

This study on potentiometric titration of polyprotic acids and bases using a glass electrode is a continuation of our paper (Maslarska V., Tencheva J., Budevsky O., Anal. Bioanal. Chem., 375, 217, 2003 [1]). The derived earlier theoretical equation was found to fit well the experimental data. A commercial software was applied and main attention was paid to the analytical result rather than to the parameters like pK-values or glass electrode constants. Specific details concerning determination of some polyprotic compounds have been discussed. The investigated species were divided into two groups depending on their acid-base strength. In both cases, calibration of the glass electrode was not necessary, since mV-mL data were used in an auto-pH-calibration procedure. Several polyprotic
compounds were analysed in water and non-aqueous media to prove the analytical applicability of the developed method.

18. Б. Цветкова, Ж. Тенчева, П. Пейков, Подбор на хроматографски условия за едновременно количествено определяне на 7-теофилин оцетната киселина и естера ѝ с пропиленгликол, Фармация, LII (1-2), 30-33, 2005.

Abstract
The choice of optimal conditions for simultaneous determination of 7-theophyllineacetic acid and its ester with polypropyleneglycol by using RP-HPLC was described. The influence of following factor on chromatographic behavior of both compounds was investigated: concentration of organic modifier, pH-value of mobile phase and possibility to ion pair formation with triethylamine as a counter ion. The dissociation constant of 7-theophyllineacetic acid was estimated by means of potentiometric titration. pKa was found to be 3.11±0.03. The absence of acid-base properties of ester was also established. The results obtained represent a preliminary stage to development of HPLC method for analysis of ester and its possible metabolic - 7-theophyllineacetic acid after proper isolation from biological matrix.


Abstract
Quantitative methods for determination of Captopril, Enalapril maleate and Hydrochlorothiazide based on potentiometric titration were proposed. A new approach for treatment of experimental data by non-linear regression was used. The validation of the methods showed very good accuracy and precision. The proposed methods were applied for quantitative determination of pharmaceuticals in substances as well as in solid dosage forms (Captopril tablets, Sopharma and Co-Renitec tablets, MSD).

20. М.Георгиева, Б.Цветкова, В.Масларска, Ж.Тенчева, Екстракционно-спектрофотометричен метод за количествено определяне на бензалкониев хлорид в троксерутин гел, Фармация, LII (1-2), 27-29, 2005.

Abstract
A simple, sensitive and selective method for the determination of benzalkonium chloride in Troxerutin gel is described. The procedure is based on extraction of this compound as an ion-pair with bromophenol blue. The formed complex is highly coloured and could easily be extracted with chloroform. The extraction is performed at pH=12.0 using sodium hydroxide (2 mol/l). The absorbance in chloroform is measured at 606 nm. The proposed spectrophotometric method is validated. The Beer’s law is obeyed between 25 and 200% (R=0.9996) of the benzalkonium chloride declared. The precision (RSD=1.362, n=6) and the accuracy (RSD=0.946, n=9) of the method are also determined. No interference of the other excipients and the active component is established.

**Abstract**

The kinetics of esterification of 7-theophyllineacetic acid with diethylene glycol monomethyl ether in the presence of dicyclohexylcarbodiimide and 4-dimethylaminopyridine as catalyst was studied. According to the known mechanism, besides the main process, the side-reaction of intramolecular rearrangement with formation of pharmacologically active N-acylurea occurs. The course of the main and the side-process was monitored by RP-HPLC with UV-detection. For that purpose, quantification of both ester and N-acylurea in the reaction mixture was performed. Influence of the concentration of the reactants (acid, alcohol and catalyst) on the progress of esterification and preparation of the by-product was investigated. Based on the obtained results, the reaction conditions leading to maximal yield of the ester and N-acylurea are proposed. The possibility of turning esterification to the synthesis of the side-product was also found. Reactions of the preparation of both the ester and N-acylurea were found to follow first-order kinetics. The rate constants of both processes were estimated.

**Цитати**


3. Dziczkowski, U Chatterjee, Route to co-acrylic modified alkyd resins via a controlled polymerization technique, Progress in Organic Coatings, 2011.

22. V. Maslarska, J. Tencheva, O. Budevsky, Quantitative determination of acids or bases mixtures by potentiometric titration, *Der Chemica Sinica*, 2, 6, 325-330 2011. I.F. 0.221

**Abstract**

Earlier proposed a general approach using data mV/mL from a potentiometric titration is tested for the quantitative determination of mixtures of mono- and poly-protic substances. The method is based on the treatment of the primary data with nonlinear regression procedure using commercial software which gives directly the analytical result. A general formula valid for every type of acid base titration (even mixtures of mono- and poly-protic substances) is used as a direct input with the applied software. Along with the analytical concentration, some specific parameters of the analyzed system are also determined (pK-values, Eo, pKw). The primary data mV/mL are transferred into pH/mL data using a self-calibration procedure, hence no preliminary pH-calibration of the glass electrode cell is necessary. The applicability of the method is proven to be correct by the analyses of a number of mixtures of mono- and poly-protic substances. The method is applied also in non-aqueous solvents and a number of sparingly soluble in water organic acids and bases have been determined successfully.

Ръководството е въведение в практиката на качествения и количествения анализ. Предназначено е да служи като учебно помагало при лабораторните упражнения по аналитична химия на студентите по фармация и е съобразено с програмата за обучение, както и със спецификата на тази дисциплина.

24. ФАРМАКОКИНЕТИКА. Основни принципи и клинични аспекти, Под редакцията на Д.Михайлова и Д.Станева-Стойчева. Венимекс, София, 2001 Глава 7. Цв.Живкова, Ж.Тенчева, Количествено определяне на лекарствени средства в биологични среди, стр.191-210

Монографията е подходяща като учебно помагало за дисциплината Фармакокинетика и биофармация, както и за модула „Анализ на лекарствени вещества и метаболити в биологични среди“ от допълнителната специализация по Клинична фармация за студенти по фармация, а също за следдипломно обучение по специалността „Клинична фармация“ на магистър-фармацевти.


Учебното помагало е предназначено за практически упражнения по аналитична химия на студенти по фармация, обучаващи се на английски език и е съобразено с новата учебна програма по тази дисциплина. Разгледани са главно методите за количествен анализ, като специално внимание е отделено на съвременните инструментални аналитични техники.