Nº 112

BIBLIOGRAFIA

Tema: TAMSULOSIN

Fecha: 25/10/99

WinSPIRS 2.1

No.	Registros	Solicitud
1	0	rofecoxib
2	0	rosiglitazone
* 3	2	tamsulosin

Registro 1 de 2 - Analytical Abstracts

TI: Highly sensitive method for the determination of tamsulosin hydrochloride in human plasma dialysate, plasma and urine by high-performance liquid chromatography-electrospray tandem mass spectrometry.
AU: Matsushima,-H; Takanuki,-K; Kamimura,-H; Watanabe,-T; Higuchi,-S
AD: Yamanouchi Pharm. Co., Drug Metabolism Lab., Itabashi-ku, Tokyo 174, Japan
CP: Japan
SO: J-Chromatogr,-B:-Biomed-Appl. 1 Aug 1997; 695(2): 317-327
JN: Journal-of-Chromatography,-B:-Biomedical-Applications
IS: 0378-4347
CO: JCBBEP
PY: 1997
LA: English
PT: Journal
AB: Plasma dialysate was treated with (+/-)-(R)-5-(3{[2-(o-ethoxyphenoxy)ethyl]amino}butyl)-2-methoxybenzenesulfonamide hydrochloride, as internal standard, and saturated NaHCO3, before extraction with ethyl acetate. Plasma and urine were treated similarly but with extraction with hexane/ethyl acetate (7:3). Each extract was evaporated to dryness, and the residue was dissolved in the mobile phase for HPLC on a 5 micro m JP2Sphere ODS-80H column (75 mm x 4.6 mm i.d.) with, as mobile phase (0.5 ml/min), methanol/50mM-acetic acid (3:2) adjusted to pH 4.0 with 50mM-ammonium acetate. Electrospray ionization MS-MS was carried out with selected reaction monitoring for tamsulosin hydrochloride and the internal standard. An in vivo protein binding study is reported. Calibration graphs were linear for 10-1000 pg/ml for plasma dialysate, 0.5-50 ng/ml in plasma and 1-100 ng/ml for urine. The intra-day RSD (n = 6) were 5.0-17.7% in dialysate, 2.4-13.3% in plasma and 3.6-18.9% in urine; the inter-day RSD was 3.3-6.7% (n = 18).
IA: tamsulosin-A: [106133-20-4]. detmn. of, in plasma and urine, by HPLC-tandem electrospray MS
IM: blood-plasma-M: detmn. of tamsulosin in, by HPLC-tandem electrospray MS;
urine-M: detmn. of tamsulosin in, by HPLC-tandem electrospray MS
IC: chromatography,-liquid,-high-performance-C: coupled with tandem electrospray MS, in pharmaceutical analysis;
mass-spectrometry,-electrospray-C: tandem, coupled with HPLC, in pharmaceutical analysis
SC: G-Pharmaceutical-Analysis
SS: 11502

AN: 5912G00094
UD: 5912

Registro 2 de 2 - Analytical Abstracts

TI: Determination of alpha1-adrenoceptor antagonists in plasma by radioreceptor assay.
AU: Yamada,-S; Tanaka,-C; Suzuki,-M; Ohkura,-T; Kimura,-R; Kawabe,-K
AD: Univ. Shizuoka, Dept. Biopharm., School Pharm. Sci., Shizuoka 422, Japan
CP: Japan
SO: J-Pharm-Biomed-Anal. Jan 1996; 14(3): 289-294
JN: Journal-of-Pharmaceutical-and-Biomedical-Analysis
IS: 0731-7085
CO: JPBADA
PY: 1996
LA: English
PT: Journal
AB: Plasma was stirred with methanol and the mixture centrifuged at 15 000 g for 15 min. The supernatant was vortex mixed with 0.01M-NaOH and diethyl ether for 1 min, centrifuged and the diethyl ether phase was evaporated to dryness under N2. The residue was dissolved in methanol and mixed with rat cerebral cortical membranes and 0.2nM-[3H]prazosin in 50mM-Tris hydrochloride buffer of pH 7.4. The mixture was incubated at 25degreeC for 1 h, the reaction was terminated by rapid filtration and the filters were washed with ice-cold buffer. The filters were extracted overnight in scintillation solution comprising toluene, Triton X-100, 2,5-diphenyloxazole and 1,4-bis[2-(5-phenyloxazolyl)]benzene and the radioactivity was determined by liquid scintillation counting. Logit-log calibration graphs were linear for 0.1-30 pmol prazosin hydrochloride per assay, 0.1-30 pmol bunazosin hydrochloride and 0.01-30 pmol tamsulosin hydrochloride with detection limits of 0.2, 0.3 and 0.05 pmol, respectively. The intra-assay RSD (n = 5) for prazosin hydrochloride were 9.1-9.2% and the inter-assay RSD (n = 5) were 5.9-6.3%.
IA: prazosin-hydrochloride-A: [19237-84-4]. detmn. of, in plasma, by liquid scintillation counting;
tamsulosin-A: detmn. of, in plasma, by liquid scintillation counting;
bunazosin-hydrochloride-A: detmn. of, in plasma, by liquid scintillation counting
IM: blood-plasma-M: detmn. of bunazosin hydrochloride, prazosin hydrochloride and tamsulosin in, by liquid scintillation counting
IC: scintillation-counting,-liquid-C: in pharmaceutical analysis
SC: G-Pharmaceutical-Analysis
SS: 10902

J. Pharmacokinet. Biopharm. **1997**, 25(3), 349–362 (Eng). Plenum Publishing Corp. A novel method is described for assessing drug bioavailability from pharmacol. data. The method is based upon a generalized model for the relation between the obsd. effect (E) and the input rate (f): E = φ(c_eA * f), where * denotes convolution, c_eA is effect site unit impulse response ("amt." of drug at the effect site resulting from the instantaneous input of a unit amt. of drug) and φ is transduction function (relates "amt." of drug at the effect site to E). The functions φ and c_eA are expressed as cubic splines for max. versatility. Pharmacol. data collected after the administration of two different doses by i.v. infusion are analyzed simultaneously to est. the function parameters. This exptl. design addresses the fact that φ and c_eA cannot be uniquely estd. from the results of a single dose expt. The unknown f from a test treatment is then estd. by applying an implicit deconvolution method to the pharmacol. data collected during that treatment. The method was tested with simulated data. The method and the model were further evaluated by application to a clin. study of verapamil (V) pharmacodynamics in 6 healthy volunteers. Simulations showed that the method is accurate and precise in the presence of a high degree of measurement error, but large intrasubject variability in the model functions can result in biased ests. of the amt. absorbed. The method produced reasonably accurate ests. of the V input rate and systemic availability (F) in the 6 human volunteers though there was a trend towards underestimation (estd. total F% 93.6 vs. the true F% of 100).

128: 212588j **HPTLC determination of isoniazid and acetylisoniazid in serum. Comparison with HPLC.** Habel, D.; Guermouche, S.; Guermouche, M. H. (Institut de Chimie, USTHB, Algiers, Algeria). *J. Planar Chromatogr.--Mod. TLC* **1997**, 10(6), 453–456 (Eng). Research Institute for Medicinal Plants. Quant. detn. of isoniazid (INH) and its acetyl metabolite (AcINH) in blood serum by high performance thin-layer chromatog. (HPTLC) was optimized. Alkalized serum samples with nicotinamide as an internal std. were deproteinized with $(NH_4)_2SO_4$ and extd. with chloroform/butanol (95:5). One-dimensional HPTLC was performed on silica gel plates with Et acetate–methanol (70:30) as a mobile phase. Quantitation was done by densitometry. Calibration curves were constructed and detection limits, precision, and repeatability for INH and AcINH anal. were established. The method was compared with HPLC and satisfactory correlation was found between data from the two techniques. The HPTLC method is sensitive and specific and was used to quantify INH and AcINH in patient blood serum.

→ 128: 212589k **Radioreceptor assay analysis of tamsulosin and terazosin pharmacokinetics.** Taguchi, Katsunari; Schafers, Rafael F.; Michel, Martin C. (Department of Medicine, University of Essen, 45122 Essen, Germany). *Br. J. Clin. Pharmacol.* **1998**, 45(1), 49–55 (Eng), Blackwell Science Ltd.. A radioreceptor assay has been developed for α_1-adrenoceptor subtypes and applied to a pharmacokinetic anal. of tamsulosin and terazosin. Young, male, healthy volunteers received 0.4 mg tamsulosin (as Omnic® modified release capsules) or 5 mg terazosin (as Flotrin® tablets) in a randomized, cross-over design. Before and after 1, 3, 5, 7, 10 and 23.5 h plasma was analyzed by radioreceptor assay using cloned human α_{1A}-, α_{1B}- and α_{1D}-adrenoceptors and specific h.p.l.c. anal. Following ingestion of tamsulosin, median peak plasma levels of 16 ng ml^{-1} were reached after 5 h and declined to 2 ng ml^{-1} at 23.5 h. The time course in the radioreceptor assay was similar, and at most time points binding to α_{1A}-adrenoceptors was significantly greater than to α_{1B}- and α_{1D}-adrenoceptors. Following ingestion of terazosin median peak plasma levels of 91 ng ml^{-1} were reached after 1 h and declined to 11 ng ml^{-1} at 23.5 h. In the radioreceptor assay binding also peaked at 1 h and declined thereafter, but even after 23.5 h considerable binding activity remained detectable at all three subtypes. At most time points binding to the α_{1A}- and α_{1D}-adrenoceptor was significantly greater than to the α_{1B}-adrenoceptor. We conclude that α_1-adrenoceptor antagonist pharmacokinetics can be monitored by radioreceptor assays in a subtype-selective manner. Tamsulosin and terazosin exhibit subtype selective receptor binding ex vivo. The discordance between terazosin blood levels as detd. by h.p.l.c. and radioreceptor assay at late time points indicates the possible involvement of metabolites in in vivo terazosin effects.

128: 212590d **Platelet aggregation in response to collagen and thrombin reliably detects the ingestion of low-dose aspirin.** Muller, T. H.; Schmidt, S.; Schunter, F.; Reil, G. H. (Institut Oldenburg, DRK-Blutspendedienst Niedersachsen, Sachsen-Anhalt, Oldenburg und Bremen, Oldenburg, Germany). *Beitr. Infusionsther. Transfusionsmed.* **1997**, 34(Transfusionsmedizin 1996/97), 105–109 (Eng), S. Karger AG. A platelet aggregation assay to detect previous aspirin ingestion was evaluated. Platelet aggregation was evaluated ex vivo in 20 aspirin-treated (100 mg single oral dose/day) patients in comparison with a control group of 20 aspirin-free donors. The results demonstrate a significant redn. in the collagen (2.5 μg/mL)-induced platelet aggregation by aspirin treatment, whereas thrombin (50 μmol/L TRAP 6)-induced platelet aggregation was not affected at all. Assessment of collagen-induced platelet aggregation relative to platelet responses of the same subject elicited either by thrombin or by a combinati... collagen and thrombin does substantially improve the rel... functional assays of aspirin.

128: 212591e **Reactivity of antineoplastic drug... tides studied by advanced mass spectrom...** Carbone, Virginia; Pocsfalvi, Gabriella; ... Antonio (International Mass Spectrome... Research Council, 80131 Naples, ... 504(Selected Topics in Mass S... ...413–425 (Eng), Kluwer Academic Publishers. The in vivo interaction of the antineoplastic drug 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) and acrolein with model peptides has been investigated to provide a detailed description of their electrophilic reactivity towards biol. macromols. Following incubation with these substances, the modified species were sepd. by HPLC and identified by fast atom bombardment mass spectrometry, whereas the reactive amino acids within the peptides structure were assigned by tandem mass spectrometry. Incubation with BCNU led essentially to the formation of an N-terminal carbamoyl deriv. that slowly decompd. to form three isomeric structures and a very minor ethylated adduct. Alkylation with acrolein gives rise to a mixt. of different adducts due to the reaction of both the double bond and the carbonyl group. Two species contg. intramol. cross-links were also obsd. These results constitute the pre-requisite for in vitro and in vivo studies on the modification of Hb in patients following treatment with antineoplastic drugs.

128: 212592f **An assessment of two gastric transport models currently used in safety pharmacology testing.** Baldrick, P.; Bamford, D. G.; Tattersall, M. L. (Department of Toxicological Research, UCB SA, B-1420 Braine-l'Alleud, Belg.). *Hum. Exp. Toxicol.* **1998**, 17(1), 1–7 (Eng), Stockton Press. The potential effects of new drugs on the digestive system can be examd. in a no. of model systems of which intestinal motility in the mouse and/or gastric emptying in the rat are examples recommended for safety pharmacol. evaluation. Intestinal motility, assessed by the transit of carmine dye in the mouse and gastric motility, assessed by stomach wt. in the rat, were examd. using a range of clin. drugs or potent pharmacol. agents known to affect gastrointestinal function. Assessment of both models in the guinea-pig was also evaluated. Activity was demonstrated with codeine, diazepam, atropine and CCK-8 (all of which inhibited gastric function). However, neither model gave consistent and reliable results with the remaining ref. compds., namely metoclopramide, bethanechol, cisapride, deoxycholate, carbachol and domperidone. In conclusion, this investigation questions the usefulness of simple models of gastrointestinal transport in the rodent as a means of detecting potential effects of a new drug on the digestive system. This finding should be of concern to the pharmaceutical industry as these simple models are routinely used as part of a regulatory safety pharmacol. "package" of studies.

128: 212593g **Modification of model membrane by new bifunctional surfactants.** Sarapuk, Janusz; Gabrielska, Janina; Przestalski, Stanislaw (Department of Physics and Biophysics, Agricultural University, 50-375 Wroclaw, Pol.). *Curr. Top. Biophys.* **1997**, 21(1), 54–57 (Eng), Wydawnictwo Protext. A no. of new bifunctional surfactants was synthesized for potential use them as compds. that can be incorporated into model or biol. membranes to protect them against lipid peroxidn. and its consequences. For that purpose the surfactants were provided with an antioxidant functional group. To anchor the surfactants in the membranes they had inbuilt hydrophobic alkyl chains of different lengths. They also differed between each other in some other details. The work contains results of studies on the interaction of the surfactants with model lipid membranes. The aim of our studies was to det. what possible concns. of surfactants can be used to ensure membrane protection without drastic changes in its properties. Model membranes used were planar lipid membranes (BLM) and liposomes.

128: 212594h **Application of spectrophotometry to evaluation of the levels and the influence of chemotherapeutic drugs on ATP of malignant cell lines.** Wang, Hongjing; Peng, Zhilan; Ding, Shining (Department of Obstetrics and Gynecology, The Second Affiliated Hospital, West China University of Medical Sciences, Chengdu, Peop. Rep. China 610041). *Huaxi Yike Daxue Xuebao* **1997**, 28(3), 300–303 (Ch), Huaxi Yike Daxue. The level and effects of ATP (ATP) in HELA and L_{929} cell lines resp. derived from human cervical carcinoma and mouse fibroma were investigated. When the cellular nos. were ≥ 2 x 10^5, the relationship between the ATP concn. and the cellular nos. was linear in both cell types. When L_{929} were incubated with cis-platinum (1x, 2x, 5x X plasma peak concn., PPC), ATP concn. was decreased ... dependently. No decrease of ATP concns. was obsd. after ... on with adriamycin (1x, 2x, 5x X PPC). The results suggest ... trophotometry is effective for studying the energy m... ence of chemotherapeutic drugs on ATP concns.

128: 212595j **Simultaneous determinat... and 8-oxo-O6-benzylguanine in ... phase high-performance liquid...** L.; Ingalls, Stephen T.; Mink... Stanton L.; Spiro, Timot... Pharmacology, Case W... USA). *J. Chromat...* (Eng), Elsev... say for th... was ...

...resp. mols. ...to 30 min occlusion of ...h of reperfusion. Vehicle or glyco... was administered i.v. immediately before the onset ...sion and every hour during the reperfusion period. Myocardial infarct size in rabbits treated with GM1292 (two glucuronic acid residues)

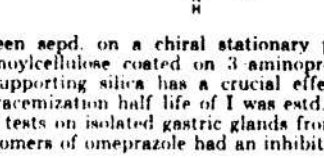
114: 74591n A novel model of solitary hepatic tumor in rats using ascites hepatoma AH13: suitability for chemotherapeutic studies. Tamura, Yoshihiro; Sakata, Yuh; Tsushima, Kenichi; Narushima, Seiko; Yamada, Yasuhide; Ogasawara, Hitoshi; Ito, Tohru; Saitoh, Soh; Suzuki, Hidekazu; Yoshida, Yutaka (Sch. Med., Hirosaki Univ., Hirosaki, Japan 036). *Jpn. J. Cancer Res.* **1990**, 81(10), 1045-51 (Eng). A highly reproducible model of a solitary hepatic tumor in rats using ascites hepatoma AH13 has been developed using a two step method which was suitable for quant. chemotherapeutic studies. Diffuse hepatic metastases were induced first by inoculation of three different ascites hepatomas, AH13, AH130 and AH7974 into the portal vein in a dose dependent fashion. Second, the induced hepatic tumor (3×10^7 cells) was minced into $1 \times 1 \times 4$ mm fragments and implanted in the liver of normal rats. In this procedure, the AH13 strain proved best suited for the generation of a solitary hepatic tumor. The growth of the solitary liver tumor using AH13 was highly reproducible. To demonstrate the suitability of this solitary hepatic tumor model for the evaluation of chemotherapy, the tumor burdened rats were treated with adriamycin (ADR) and mitomycin C (MMC). The redn. in tumor size was proportional to dosage, and the statistical significance of the differences between the treatment group and control group was proportional to dosage. A synergistic effect of ADR and MMC on the tumor also was demonstrated. This model should prove to be a useful tool for the testing of newly developed treatments of hepatic cancer.

114: 74592p Liquid chromatographic determination of 6-thiopurine metabolites formed in vitro in electrochemical and enzymic oxidative activation. Zhu, Shi Min; Brajter-Toth, Anna (Dep. Chem., Univ. Florida, Gainesville, FL 32611 USA). *Anal. Chim. Acta* **1990**, 237(2), 305-10 (Eng). A micellar liq. chromatog. method was developed for the sepn. of the oxidn. metabolites of 6-thiopurine formed in vitro by electrochem. and enzymic activation. Electrochem. activation was carried out with an electrochem. cell online with the chromatograph. In the potential range 0.4-0.8 V vs. Pd, intermediate purine 6-sulfenic acid was detected together with purine 6-sulfinic acid and 6-thiopurine disulfide. At potentials >0.8 V, purine-6-sulfonic acid was detected and the oxidn. of 6-thiopurine was completed. Intermediates and products formed in the horseradish peroxidase were similar to electrochem. oxidn. at <0.8 V. Detection of sulfenic acid in the enzymic oxidn. supports earlier results which indicated that this metabolite may have biol. significance. The results also provide some insight into the enzymic oxidn. pathway.

114: 74593q Screening and detection of nimetazepam and its major metabolites. Schoelermann, K.; Schuetz, H. (Inst. Rechtsmed., Justus Liebig Univ., D-6300 Giessen, Fed. Rep. Ger.). *Beitr. Gerichtl. Med.* **1990**, 48, 657-65 (Ger). Nimetazepam and its metabolites 7-aminonimetazepam, *N*-desmethylnimetazepam (nitrazepam), 2-methylamino-5-nitrobenzophenone, 5-amino-2-(methylamino)benzophenone, and 2-amino-5-nitrobenzophenone were detd. in human urine using TLC, GC, mass spectrometry, and UV- and IR-spectrometry.

114: 74594r Analysis of N-methyl-4-piperidinyl benzilate. Hoehn, H.; Goeber, B.; Gabrio, T. (Wissenschaftsbereich Pharm., Humboldt-Univ., DDR 1120 Berlin, Ger. Dem. Rep.). *Pharmazie* **1990**, 45(8), 576-8 (Ger). Attempts at the photometric detn. of the title anticholinergic compd. (I) in model solns. (MeOH or concd. H_2SO_4) gave unsatisfactory results. A capillary column gas-chromatog. method with thermionic detection was a suitable method for detg. I in the low nanogram range. Since this method could distinguish I from decompn. products in model solns. and in (unspecified) biol. material, it is considered to be sufficiently precise for pharmacokinetic studies.

114: 74595s Resolution of the enantiomers of omeprazole and some of its analogs by liquid chromatography on a trisphenylcarbamoylcellulose-based stationary phase. The effect of the enantiomers of omeprazole on gastric glands. Erlandsson, Per; Isaksson, Roland; Lorentzon, Pia; Lindberg, Per (Chem. Cent., Univ. Lund, S-221 00 Lund, Swed.). *J. Chromatogr.* **1990**, 532(2), 305-19 (Eng). The enantiomers of omeprazole (I) and some of its

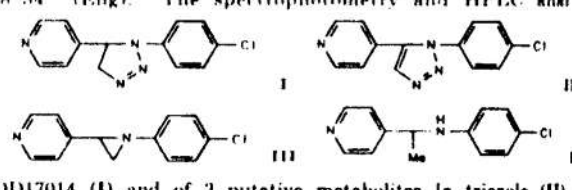


I

analogs have been sepd. on a chiral stationary phase comprising trisphenylcarbamoylcellulose coated on 3-aminopropyl silica. The nature of the supporting silica has a crucial effect on the sepns. obtained. The racemization half life of I was estd. to be $1.3 \cdot 10^7$ h at 37°. In vitro tests on isolated gastric glands from rabbits showed that both enantiomers of omeprazole had an inhibitory effect on acid formation.

114: 74596t Analysis of amine metabolites by high-performance liquid chromatography on silica gel with a nonaqueous ionic eluent. Cashman, John R.; Yang, Zi-Cheng (Dep. Pharm. Chem., Univ. California, San Francisco, CA 94143-0446 USA). *J. Chromatogr.* **1990**, 532(2), 405-10 (Eng). Analyses of tertiary amines, zimelidine, *N,N*-dimethylaniline, chlorpheniramine, and brompheniramine, and their oxidative metabolites by HPLC was described. The mobile phase was perchloric acid and methanol. Metabolites were extd. with dichloromethane; detection was at 260 nm; the detection limit was 5-20 ng/mL and the recovery was 90-100%.

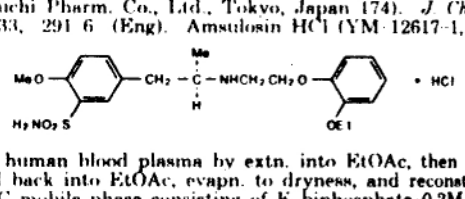
114: 74597u Triazolines. XXII. Chromatography of 1-phenyl-5-(4-pyridyl)-Δ^2-1,2,3-triazolines and related 1,2,3-triazoles, a new class of anticonsulvant agents. Stevenson, P. J.; Hauksdottir, R.; Kadaba, P. K.; Damani, L. A. (Chelsea Dep. Pharm., King's Coll. London, London, UK SW3 6LX). *J. Chromatogr.* **1990**, 533, 248-54 (Eng). The spectrophotometry and HPLC anal. of



I II III IV

ADD17014 (I) and of 3 putative metabolites [a triazole (II), an aziridine (III), and an imine (IV)] were studied. I and IV undergo breakdown at acidic or neutral pH, and so anal. procedures must be developed that will prevent ex vivo changes of these anticonvulsants in blood samples. I and its metabolites can be detd. in rat blood by extn. into Et_2O followed by sepn. on a reversed phase Spherisorb 5 ODS column, with a mobile phase composed of acetonitrile-MeOH-McIlvaine's phosphate buffer (pH 8.0, 0.005M) in the ratio 30:30:40. The absorption max. of these compds. are 290, 250, 235, and 236 nm, for I, II, III, and IV, resp.

114: 74598v Sensitive method for the determination of amsulosin in human plasma using high-performance liquid chromatography with fluorescence detection. Soeishi, Yoshiaki; Kobori, Mikio; Kobayashi, Shinichiro; Higuchi, Saburo (Appl. Pharmacol. Lab., Yamanouchi Pharm. Co., Ltd., Tokyo, Japan 174). *J. Chromatogr.* **1990**, 533, 291-6 (Eng). Amsulosin HCl (YM-12617-1, I) can be



I

detd. in human blood plasma by extn. into EtOAc, then into 0.01 M HCl and back into EtOAc, evapn. to dryness, and reconstitution in an HPLC mobile phase consisting of K biphosphate-0.2M H_3PO_4-acetonitrile (7:7:5). Sepn. is effected on a Nucleosil 5C_{18} column equipped with an RF-535 fluorescence detector. Detection is at 23 nm (excitation) and 325 nm (emission). The detection limit was 0.5 ng/mL, and the method was precise enough for carrying out pharmacokinetic studies in humans.

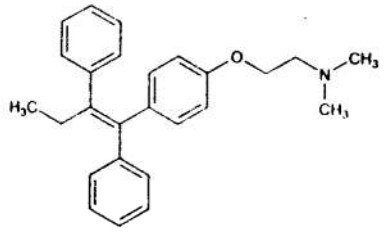
114: 74599w High-performance liquid chromatographic determination of diacetolol enantiomers. Piquette-Miller, M.; Foster, R. T. (Fac. Pharm. Pharm. Sci., Univ. Alberta, Edmonton, AB Can. T6G 2N8). *J. Chromatogr.* **1990**, 533, 300-3 (Eng). Enantiomers of diacetolol (the chiral metabolite of acebutolol) can be detd. in blood and urine by extn. (details not given), derivatization with *S*(+)-1-(naphthyl)ethyl isocyanate, and normal phase HPLC (details not given). The method is suitable for pharmacokinetic studies.

114: 74600q Simultaneous assay of propranolol, diltiazem and metabolites of diltiazem in human plasma by liquid chromatography. Ververs, F. F. T.; Schaefer, H. G.; Lefevre, J. F.; Lopez, M.; Derendorf, H. (Coll. Pharm., Univ. Florida, Gainesville, FL 32610 USA). *J. Pharm. Biomed. Anal.* **1990**, 8(6), 535-9 (Eng). An HPLC method for the detn. of propranolol and diltiazem and diltiazem metabolites (deacetyldiltiazem, *N*-dimethyldiltiazem) in human blood plasma is described. Alkalized samples with the internal std. imipramine were extd. with hexane-butanol (90:4), the org. phase was reextd. with 5 mM H_2SO_4, and the new aq. phase was analyzed on a reversed-phase Nucleosil C_{18} column. The mobile phase consisted of acetonitrile-methanol-ammonium chloride-triethylamine (24:40:36:0.08). UV detection was set at 238 and 236 nm. The calibration was linear in the ranges of 5-200 ng/mL for diltiazem, 5-100 ng/mL for deacetyldiltiazem, 10-200 ng/mL for *N*-demethyldiltiazem, and 5-100 ng/mL for propranolol. The coeffs. of variation were acceptable. The method was used in a pharmacokinetic study in a healthy man given diltiazem and propranolol.

114: 74601r Direct injection analysis of diuretic and anti-inflammatory drugs on a shielded hydrophobic phase column. Santasania, C. T. (Supelco, Inc., Bellefonte, PA 16823 USA). *J. Chromatogr.* **1990**, 13(13), 2605-31 (Eng). A shielded hydrophobic phase (SHP) column was used for the direct injection anal. of drugs in blood serum. Gradient elution gave the best sepn.; however, isocratic sepn. is possible. The mobile phase pH was found to play a major role in the sepn.; ionic strength had a lesser influence. Quantitation of the drugs of interest was possible over several orders of magnitude. Inter- and intra-day recoveries showed values of 100%. A drug contg. serum sample was analyzed, using the described method, and the results were compared to a reference chromatog. method.

114: 74602s Quantitative determination of bonnecor and its metabolites in biological fluids by HPLC. Beloborodov, V. L.; Rodionov, A. P.; Kosilova, E. E.; Ignatova, N. A.; Zalesskaya, A.; Gritsenko, A. N.; Kolesnik, Yu. A. (IMMI, Moscow, USSR). *Khim. Farm. Zh.* **1990**, 24(11), 83-6 (Russ). A procedure is proposed for quant. anal. of bonnecor (I), a new antiarrhythmic agent, and its metabolites in biol. fluids by applying HPLC. Various modes of prepg. biol. samples to be analyzed are described and comparatively assessed. Optimal conditions are given for chromatog. sepn. of I and its metabolites. The procedure for measuring the agent and its metabolites in blood may be useful for pharmacokinetic and biopharmaceutical studies.

(1967). Review of biochemistry: R. I. Nicholson *et al.*, *Adv. Sex Horm. Res.* **4**, 119-152 (1980); of pharmacology and use in breast cancer: V. C. Jordan *et al.*, *Cancer Treat. Rep.* **64**, 745-759 (1980); of pharmacokinetics and metabolism: V. C. Jordan, *Breast Cancer Res. Treat.* **2**, 123-138 (1982); of chemistry, pharmacology and clinical uses: B. J. A. Furr, V. C. Jordan, *Pharmacol. Ther.* **25**, 127-205 (1984). Brief review of use in mastalgia: I. S. Fentiman, *Drugs* **32**, 477-480 (1986). Review of toxicities and drug resistance: V. C. Jordan, *Ann. Rev. Pharmacol. Toxicol.* **35**, 195-211 (1995).



Crystals from petr. ether, mp 96-98°.

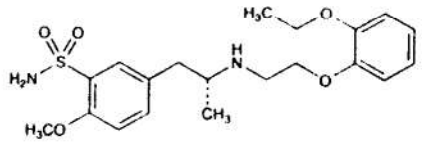
Citrate, $C_{26}H_{29}NO.C_6H_8O_7$. *ICI-46474*. **Kessar, Noltam, Salvadex, Nourytam, Tamofen, Tamoxasta, Zemide.** Fine, white, odorless crystalline powder, mp 140-142°. Slightly sol. in water, sol. in ethanol, methanol, acetone. Hygroscopic at high relative humidities. Sensitive to uv light. LD_{50} in mice, rats (mg/kg): 200, 600 i.p.; 62.5, 62.5 i.v.; 3000-6000, 1200-2500 orally (Furr, Jordan).

cis-Form base, mp 72-74° from methanol.

cis-Form citrate, $C_{26}H_{29}NO.C_6H_8O_7$. *ICI-47699*. mp 126-128°.

THERAP CAT: Antiestrogen. Palliative treatment of breast cancer.

9217. Tamsulosin. *(R)-5-[2-[[2-(2-Ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide; ansulosin.* $C_{20}H_{28}N_2O_5S$, mol. wt. 408.52. C 58.80%, H 6.91%, N 6.86%, O 19.58%, S 7.85%. Specific α_1-adrenoceptor antagonist. Prepn: K. Imai *et al.*, Eur. pat. **Appl. 34,432**; *idem*, U.S. pat. **4,703,063** (1981, 1987 both to Yamanouchi). Pharmacology: K. Honda *et al.*, *Arch. Pharmacol.* **328**, 264 (1985); of racemate and enantiomers: K. Honda *et al.*, *ibid.* **336**, 295 (1987). HPLC determn. in plasma: Y. Soeishi *et al.*, *J. Chromatog.* **533**, 291 (1990). Clinical trials in micturition difficulty: K. Kawabe, I. Niijima, *Urol. Int.* **42**, 280 (1987); in benign prostatic hypertrophy: K. Kawabe *et al.*, *J. Urol.* **144**, 908 (1990).



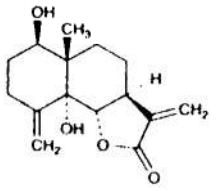
(−)-Form hydrochloride, $C_{20}H_{28}N_2O_5S.HCl$. *YM-12617*, mp 254-256°.

(*R*)-Form hydrochloride, *EY-25335I*, *YM-12617-1*, *YM-612*, *Harnal*, mp 228-230°, $[\alpha]_D^{24}$ −4.0° (c = 0.35 in methanol).

(*S*)-Form hydrochloride, *YM-12617-2*, mp 228-230°, $[\alpha]_D^{24}$ +4.2° (c = 0.36 in methanol).

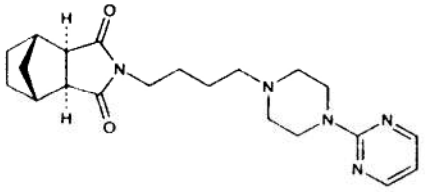
THERAP CAT: In treatment of benign prostatic hypertrophy.

9218. Tanacetin. *[3aS-(3aα,5aβ,6β,9aα,9bβ)]-Decahydro-6,9a-dihydroxy-5a-methyl-3,9-bis(methylene)naphtho[1,2-b]furan-2(3H)-one;* 1β,5α-dihydroxy-6β,7αH-eudesma-4(15),11(13)-dien-6,12-olide. $C_{15}H_{20}O_4$, mol. wt. 264.32. C 68.16%, H 7.63%, O 24.21%. Isoln. from seed, herb, and flowers of *Tanacetum vulgare* L. (*Compositae*): Hornolle, *J. Pharm. Chim.* **7**, 57 (1845); Jaretzky, Kuhne, *Arch. Pharm.* **271**, 353 (1933); Suchy, *Coll. Czech. Chem. Commun.* **27**, 1058 (1962). Structure and absolute config.: Samek *et al.*, *ibid.* **38**, 1971 (1973).



Crystals, mp 205°. $[\alpha]_D^{22}$ +179.5° (c = 2.3 in ethanol).

9219. Tandospirone. *(3aα,4β,7β,7aα)-Hexahydro-2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-4,7-methano-1H-isoindole-1,3(2H)-dione; (1R*,2S*,3R*,4S*)-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-2,3-bicyclo[2.2.1]heptanedicarboximide.* $C_{21}H_{29}N_5O_2$, mol. wt. 383.49. C 65.77%, H 7.62%, N 18.26%, O 8.34%. Serotonin ($5\text{-}HT_{1A}$) receptor agonist. Prepn: K. Ishizumi *et al.*, Eur. pat. **Appl. 82,402**; *idem*, U.S. pat. **4,507,303** (1983, 1985 both to Sumitomo); *idem et al.*, *Chem. Pharm. Bull.* **39**, 2288 (1991). Behavioral pharmacology: C. A. Sanneraud *et al.*, *Drug Alc. Depend.* **32**, 195 (1993). Clinical efficacy in treatment of bulimia: H. Tamai *et al.*, *Int. J. Obesity* **14**, 289 (1990). Clinical evaluation of potential adverse effects: M. Suzuki *et al.*, *Japan. J. Psychopharmacol.* **13**, 213 (1993); of abuse liability: S. M. Evans *et al.*, *J. Pharmacol. Exp. Ther.* **271**, 683 (1994). Review of pharmacology: P. A. Seymour *et al.*, *Prog. Clin. Biol. Res.* **361**, 453-460 (1990).



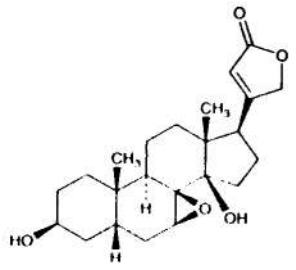
Crystals from toluene/*n*-hexane, mp 112-113.5°.

Citrate, $C_{21}H_{29}N_5O_2.C_6H_8O_7$. *SM-3997*, mp 169.5-170°.

Hydrochloride, $C_{21}H_{29}N_5O_2.HCl$, crystals from isopropanol, mp 227-229°.

THERAP CAT: Anxiolytic; antidepressant.

9220. Tanghinigenin. *(3β,5β,7β)-7,8-Epoxy-3,14-dihydroxycard-20(22)-enolide.* $C_{23}H_{32}O_5$, mol. wt. 388.50. C 71.11%, H 8.30%, O 20.59%. Isoln. from glucosides: Sigg *et al.*, *Helv. Chim. Acta* **38**, 166 (1955). Structure: Flury, Reichstein, *Ann. Chim. (Rome)* **53**, 23 (1963); Flury *et al.*, *Helv. Chim. Acta* **48**, 1113 (1965). Toxicity study: Chen, Henderson, *J. Pharmacol. Exp. Ther.* **111**, 365 (1954).



Prisms from acetone + petr. ether, mp 187-188°. $[\alpha]_D^{25}$ +14.1° (c = 1.138 in chloroform); uv max: 217 nm (log ε 4.22). LD_{50} i.v. in cats: 1 mg/kg (Chen, Henderson).

Acetate, $C_{25}H_{34}O_6$. *acetyltanghinigenin.* Prisms from acetone + petr. ether, mp 241-243°. $[\alpha]_D^{24}$ +14.9° (c = 1.075 in chloroform).

3-[(2-*O*-Acetyl-6-deoxy-3-*O*-methyl-α-L-glucopyranosyl)-oxy]-. $C_{32}H_{46}O_{10}$. *tanghinin.* From the seed of *Tanghinia*