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BIBLIOGRAFIA

Tema: Disolución de Ketoprofeno usando arginina como coadyuvante en la preparación de inyectables

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04

Quantitative Fourier transform infrared/attenuated total reflectance analysis of ketoprofen in some pharmaceutical formulations.
Van Overbeke, A.; Baeyens, W.; Van den Bossche, W. (Laboratory of Drug Analysis, Department of Pharmaceutical Analysis, Faculty of Pharmaceutical Sciences, University of Ghent, Harelbekestraat 72, Ghent B-9000, Belg.). Vib. Spectrosc., 9(2), 121-30 (English) 1995. CODEN: VISPEK. ISSN: 0924-2031.
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J Microencapsul 1992 Jul-Sep;9(3):365-73

Preparation and in vitro evaluation of slow release ketoprofen microcapsules formulated into tablets and capsules.

el Khodairy KA, Eshra AG, Nada AH, Mortada SA

Department of Industrial Pharmacy, Faculty of Pharmacy, Alexandria University, Egypt.

Ketoprofen powder was encapsulated with Eudragit RL/RS polymer solutions in isopropanol-acetone 1:1, using a simple and
rapid method. Microcapsules were prepared using Eudragit solutions with different RL/RS ratios. The encapsulation process
produces free-flowing microcapsules with good drug content and marked decrease in dissolution rate. The retardation in
release profile of ketoprofen from microcapsules was a function of the polymer ratio employed in the encapsulation process. In
vitro release of ketoprofen from microcapsules either filled in gelatin capsules or compressed into tablets, using calcium sulphate
as diluent, confirmed the efficiency of the encapsulation process for preparing prolonged release medication. A capsule
formulation with optimum sustained-release profile was suggested.

Sem Hop 1983 Dec 12;59(46):3187-90

[Pharmacokinetic profile of a slow-release ketoprofen preparation].

[Article in French]

Flouvat B, Stheneur A, Massias P

Kinetics of ketoprofen release in man from a sustained-release preparation (150 mg) and from capsules (3 X 50 mg) were
studied comparatively in 10 healthy adults. Bioavailability of the slow-release preparation is similar to that of capsules : surfaces
under the serum concentration curves and urinary elimination were found to be identical. In the sustained-release preparation
the immediately available layer (75 mg) ensures achievement of maximal serum concentrations amounting to 59% of those
obtained with capsules, after the same time interval. The slow-release layer (75 mg) produces higher serum concentrations from
the third hour on, justifying administration of the formulation in two daily doses.

Pathol Biol (Paris) 1998 May;46(5):355-9

[Impact of the method and timing of administration on the systemic transport of ketoprofen]

[Article in French]

Delhotal Landes B, Decout N, Molinier P, Flouvat B

Laboratoire de Toxicologie et de Pharmacocinetique, Hopital Ambroise Pare, Boulogne-Billancourt, France.

The pharmacokinetics of the non-steroidal antiinflammatory drugs are influenced by circadian rhythms and ketoprofen (K)
absorption by food, to investigate the influence of these two factors, 12 subjects were treated, in random order, orally by a fast
release tablet (FR 100 mg), by a fast-slow release tablet (FSR 150 mg) and by an intramuscular solution (i.m. 100 mg). The 3
treatments were administered, with a standardized meal, at 8 h a.m and 8 h p.m, and also at 1 h p.m with FR. The daily dosing
was 300 mg by oral administration and 200 mg by i.m. route. Serum concentration profiles of K were determined by HPLC.
The pharmacokinetic parameters of K were not modified by the time of intramuscular injection. The oral absorption of K
(Tmax) was significantly delayed at 1 h p.m and more even at 8 h p.m. The maximal serum concentration (Cmax) was
significantly decreased at 1 h p.m (about 50%, $p < 0.001$) and also at 8 h p.m. The oral bioavailability, evaluated by the area
under the K serum concentration curve, was not modified, those of FSR was significantly lower than FR (6%, $p < 0.05$). This
study shows that the time of K administration delayed the Tmax and food decreased the Cmax without loss of bioavailability.

Publication Types:

Clinical trial
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Improvement of Dissolution Efficiency of Ketoprofen by Solvent Deposition Technique.

Author(s)

Chowdary, K.P.R.
Krishna, S. Rama

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Title

Physical characterstics and dissolution kinetics of solid dispersions of ketoprofen and polyethylene glycol 6000.

Author(s)

Margarit, M.V.
Rodriguez, I.C.
Cerezo, A.

Journal Info

International journal of pharmaceutics.
AUG 01 1994 v 108 n 2
101

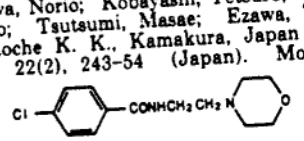
115: 99108u **Pharmacokinetics of fluocinolone acetonide in patch versus cream formulations.** Broggini, M.; Benvenuti, C.; Botta, V.; Broccali, G. (Med. Dep., Filippo del Ponte Hosp., Varese, Italy). *Int. J. Clin. Pharmacol. Res.* 1991, 11(1), 17–21 (Eng). The pharmacokinetics of the fluocinolone acetonide patch contg. 8 mcg/cm² and a 0.025% cream were studied in a cross–over trial in 12 healthy volunteers (6 male and 6 female, mean age 24.9 yr). Each subject was treated with 0.8 mg of both fluocinolone acetonide formulations for 12 h on non–consecutive days. Minor fluctuations in the plasma profile after patch application were obsd., even if no significant difference was found between the two formulations with regard to peak plasma concn., time to reach peak levels, area under the concn. curve, and half–life.

115: 99109v **Improvement of dissolution efficiency of ketoprofen by solvent deposition technique.** Chowdary, K. P. R.; Krishna, S. Rama (Dep. Pharm. Sci., Andhra Univ., Waltair, India). *Indian J. Pharm. Sci.* 1990, 52(6), 269–71 (Eng). Solvent deposited systems of ketoprofen using different excipients showed marked increase in the dissoln. rate and efficiency. Water insol. excipients gave fast dissoln. when compared to water sol. excipients.

115: 99110p **Preparation and evaluation of cellulose acetate microcapsules of theophylline.** Chowdary, K. P. R.; Ratna, J. Vijaya (Dep. Pharm. Sci., Andhra Univ., Waltair, India). *Indian J. Pharm. Sci.* 1990, 52(6), 279–81 (Eng). Theophylline was microencapsulated with cellulose acetate by a complex emulsion method and the microcapsules were studied. Controlled drug release which depended on percent coat material and size of the microcapsules and good correlation between percent coat material and T_{50} value were obsd. Drug release mechanism was found to be of diffusion type. Release followed first order kinetics.

115: 99111q **Effect of food on the bioavailability of cyclandelate from commercial capsules.** Kaniwa, Nahoko; Ogata, Hiroyasu; Aoyagi, Nobuo; Ejima, Akira; Takahashi, Terutaka; Uezono, Yuko; Imazato, Yuu (Div. Drugs, Natl. Inst. Hyg. Sci., Tokyo, Japan 158). *Clin. Pharmacol. Ther. (St. Louis)* 1991, 49(6), 641–7 (Eng). The bioavailability of five capsules of cyclandelate that are com. available in Japan was detd. in ten healthy volunteers by measuring mandelic acid (a main metabolite of cylandelate) excreted in the urine. Bioinequivalence among the five capsules was demonstrated. The relative cumulative excretion of mandelic acid of the most poorly bioavailable capsule was 38% of the most highly bioavailable capsule. The effect of food on the bioavailability of these two capsules was investigated by use of two different kinds of food, one contg. fat and one contg. high carbohydrates but very low fat. The bioavailability of the two capsules was increased when subjects consumed both types of food before drug administration, although there was a greater effect on bioavailability with food contg. fat. This suggests that the absorption of cyclandelate was incomplete in fasting subjects, even from the capsule with the highest bioavailability. Bioinequivalence between the two capsules remained after postprandial drug administration.

115: 99112r **Physicochemical properties and stability of moclobemide.** Ogawa, Norio; Kobayashi, Tetsuro; Nakai, Sachihiko; Takahashi, Naoko; Tsutsumi, Masae; Ezawa, Toshikazu (Res. Cent., Nippon Roche K. K., Kamakura, Japan 247). *Iyakuhin Kenkyu* 1991, 22(2), 243–54 (Japan). Moclobemide (I), a



I

monoamine oxidase (MAO) inhibitor, was subjected to elemental anal., and UV, IR, NMR, and mass spectrometric analyses, as well as to measurements of its physicochem. properties, i.e., soly., partition coeff., pKa, m.p., thermal anal., polymorphism, etc. Prior to the initiation of the stability test of I, two degrdn. products formed under severe conditions were isolated and identified. The stability of I was mainly studied by TLC and HPLC. I in the solid state was very stable to heat, moisture, and light. In aq. soln., I was stable in the region of pH 3–9.

115: 99113s **The interconversion of the polymorphic forms of chloramphenicol palmitate (CAP) as a function of environmental temperature.** De Villiers, M. M.; Van der Watt, J. G.; Lotter, A. P. (Dep. Pharm., Potchefstroom Univ., Potchefstroom, 2520 S. Afr.). *Drug Dev. Ind. Pharm.* 1991, 17(10), 1295–303 (Eng). When polymorph B of CAP is heated at 82° for 1600 min, it changes completely to the less sol. and less bioavailable polymorph A. When polymorph C, the most sol. polymorph, is grinded for a prolonged period, it changes to polymorph A through B. The effect of the environmental temp. on the interconversion of polymorph C was investigated. This was done to det. the effect that heat generated during grinding could have on polymorph C. Samples of polymorph C was kept at 50 and 75° resp. At predetd. intervals samples were withdrawn and DSC curves and x–ray powder diffractograms recorded. Both samples changed to polymorph B but only the sample kept at 75° changed into A during the time the expt. was run. Therefore temp. control during storage and handling, esp. grinding, on polymorph C and B is recommended to prevent conversion to the poorly sol. and less bioavailable polymorph A.

115: 99114t **Effect of dye content on point of zero charge of anionic lake dyes.** Desai, Archana; White, Joe L.; Hem, Stanley L.; Peck, Garnet E. (Dep. Ind. Phys. Pharm., Purdue Univ., West Lafayette, IN 47907 USA). *Drug Dev. Ind. Pharm.* 1991, 17(10), 1405–9 (Eng). The pure dye content of FD&C yellow lake no. 5 and FD&C red lake no. 40 was inversely related to the point of zero charge. The effect of the adsorbed anionic dye on the zeta potential of aq. suspensions of FD&C yellow lake no. 5 at pH 5 was

115: 99115u **A new predictive equation for the solubility of drugs based on the thermodynamics of mobile disorder.** Ruell, Paul; Rey–Mermet, Catherine; Buchmann, Michel; Nam Tran Ha Kesselring, Ulrich W.; Huyskens, P. L. (Sch. Pharm., Univ. Lausanne, CH–1015 Lausanne, Switz.). *Pharm. Res.* 1991, 8(7), 840–50 (Eng). The thermodn. of mobile disorder rejects the statistical model of the quasi–lattice for liqs. Because of the perpetual change of neighbors, during the obsd. time of thermodn. of the order of seconds, each mol. of a given kind in a soln. has experienced the same environment and had at its disposal the same mobile vol. The domain is not localizable and not orientable. Each mol. group perpetually "visits" successively all parts of this domain. The highest entropy is obtained when the groups visit all the parts of the domain without preference. H–bonds are preferential contacts with given sites of the neighbors that cause deviations with respect to the "random" visiting, thereby decreasing the entropy. The quantitative development of these ideas leads to equations describing the effect of solvent–solvent, solute–solvent, and solute–solute hydrogen bonds on the chem. potential of the solute. A universal equation predicting the soly. of drugs in a given solvent is derived. The effect of H–bonds is governed not by "soly. parameters" but by stability consts. from which the order of magnitude can be estd. From the sole knowledge of the soly. of methylparaben in pentane, the method predicts correctly the order of magnitude of its soly. in 26 other solvents, including alcs. and water.

115: 99116v **Dodecyl N,N–dimethylamino acetate and Azone enhance drug penetration across human, snake, and rabbit skin.** Hirvonen, Jouni; Rytting, J. Howard; Paronen, Pertti; Urtti, Arto (Dep. Pharm. Technol., Univ. Kuopio, SF–70211 Kuopio, Finland). *Pharm. Res.* 1991, 8(7), 933–7 (Eng). The effectiveness of the penetration enhancers, dodecyl *N,N*–dimethylamino acetate (DDAA) and Azone, on pretreated human epidermis for the permeation of model drugs, indomethacin, 5–fluorouracil, and propranolol–HCl, was studied in vitro diffusion cells. Snake skin (*Elaphe obsoleta*) and rabbit pinna skin were compared as possible models for human skin. The drug concns. were analyzed by HPLC. With all skins and all model drugs, DDAA increased drug permeability at least as well as Azone, and in most cases it was a more effective permeation enhancer. The relative permeation improvement in human, snake, and rabbit skin were 10– to 10–, 5– to 50–, and 30– to 120–fold, resp. Tritiated water served as an indicator of skin condition. Its penetration in the skin samples was independent of the drugs used, and both penetration enhancers significantly increased the flux of tritiated water through all skins. Thus, DDAA and Azone significantly increased the permeation of lipophilic and hydrophilic model compds. Rabbit pinna skin was a poor model for human skin in vitro, while snake skin was much closer to human skin in terms of transdermal permeability. In most cases drug permeability decreased in the order rabbit ≫ human > or < snake.

115: 99117w **Structural effects on the binding of amine drugs with the diphenylmethyl functionality to cyclodextrins. A microcalorimetric study.** Tong, Wei Qin; Lach, John L.; Ong, Ting Fong; Guillory, J. Keith (Coll. Pharm., Univ. Iowa, Iowa City, IA 52242 USA). *Pharm. Res.* 1991, 8(7), 951–7 (Eng). Microcalorimetry has been employed to evaluate the stability constants and enthalpy changes assocd. with complex formation between α–, β– and γ–cyclodextrin (CD) and a group of amine compds. having the diphenylmethyl functionality. Data from thermal titrations of the compds. were analyzed using nonlinear least squares. The standard energy decrease accompanying the formation of inclusion complexes is generally due to a neg. std. enthalpy change ($\Delta H°$). The standard entropy change ($\Delta S°$) was neg., except in the case of complexes formed with γ–CD. Of the 13 compds. studied, only 2 formed complexes with 1:2 (compd.–β–CD) stoichiometry, terfenadine and cinnarizine–2HCl. All the others formed 1:1 complexes. The structural effect on the stability consts., thermodn., and microcalorimetric results was explored by relating the calorimetric results to the geometry was explored by relating the calorimetric results to the chem. structures of the guest mols. and the cavity sizes of the CD mols. The results suggest that one of the Ph groups of the diphenylmethyl functionality resides in the CD cavity and is in van der Waals contact with the inside wall of the CD cavity. In the case of α– and β–CDs, van der Waals interaction dominates the stabilization. On the other hand, the interaction between the compds. and γ–CD is largely entropically driven. Adipheniline forms a more stable complex with β–CD than procaine, suggesting that hydrogen bonding to the carbonyl oxygen by the hydroxyl group on the rim of the CD ring can influence the stability of the binding interaction.

115: 99118x **Cyclodextrins in drug formulations: prostaglandin** Szejtli, Jozsef (Cyclolab Cyclodextrin Res. Dev. Lab., 1045 Budapest, Hung.). *Pharm. Technol.* 1991, 15(6), 36, 38, 40, 42, 44 Cyclodextrins (CDs) and some of their derivs. used for the encapsulation of many hydrophobic and/or unstable drugs are discussed. Drugs thus complexed typically are easily water more sol., which improves their bioavailability. In some cases several orally administered drugs and some parenterals are marketed CD–complexed form. For virtually any type of drug formulation can find at least one CD or CD deriv. that can advantageously modify the properties of the drug. Some of the advances made with CDs to reformulate drugs are described.

115: 99119y **Chemical properties–dissolution relationship behavior in solution of the diclofenac/N–(2–hydroxyethyl) pyrrolidine salt (DHEP).** Fini, A.; Fazio, G.; Orienti, I.; Zecchi, V.; Rapaport, I. (Inst. Sci. Chim., I–40127 Bologna, Italy). *Acta Helv.* 1991, 66(7), 201–3 (Eng). The behavior in soln. of the salt formed between diclofenac and *N*–(2–hydroxyethyl) pyrrolidine

121: **91543k Controlled release of triamterene from poly(DL-lactide-co-glycolide) microspheres.** Ouellette, Amy D.; Peppas, Nicholas A. (Inst. Biosci. Bioeng., Rice Univ., Houston, TX 77251 USA). *Mater. Res. Soc. Symp. Proc.* **1994,** 331(Biomaterials for Drug and Cell Delivery), 91–6 (Eng). Release of triamterene from 150–3000-μm poly(DL-lactide-co-glycolide) (PLGA) microspheres was investigated in vitro as a function of lactic acid/glycolic acid (LA/GA) copolymer ratio and drug loading both with free microspheres and with microspheres embedded in a silicone matrix. Biphasic release consisting of diffusion controlled release followed by erosion controlled release corresponding to polymer degrdn. was obsd. in all samples. Drug release from PLGA 50:50 copolymer microspheres was 3-fold faster than the release from PLGA 75:25 microspheres for the higher drug loading (20 wt%) and slightly faster for the lower drug loading (10 wt%). Release rates from spheres contg. the higher drug loading were approx. one order of magnitude faster than release from spheres contg. the lower drug loading for the same PLGA copolymer. The same qual. results were obsd. for the spheres embedded in silicone matrixes; however, the overall release was much slower. The release behavior may be altered by changing LA/GA copolymer ratio, drug loading, and microsphere environment to obtain the desired release characteristics.

121: **91544m Compatibility of cyclizine lactate solutions with chloride ion.** Dwyer, P. J.; Weir, P. J.; Ireland, D. S.; Taylor, C. G. (Quality Control Lab., Countess Chester Hosp., Chester, UK CH2 1BQ). *Anal. Proc.* **1994,** 31(5), 157–8 (Eng). The compatibility of an anti-emetic with the Cl^- of an analgesic was investigated by means of HPLC and UV-visible spectrophotometry. The soly. of the anti-emetic, cyclizine, deviated from theor. values as a result of supersatn. and the effect of counter ions.

121: **91545n Protein kinase C inhibitors suppress LPS-induced TNF production in alveolar macrophages and in whole blood: the role of encapsulation into liposomes.** Tschaikowsky, Klaus (Respiratory Biology Program, Department of Environmental Science and Physiology, Harvard School of Public Health, Boston, MA 02115 USA). *Biochim. Biophys. Acta* **1994,** 1222(1), 113–21 (Eng). Tumor necrosis factor (TNF) is a pivotal mediator of endotoxin shock, but the regulation of lipopolysaccharide (LPS)-induced TNF prodn. in different populations of mononuclear cells has not been fully clarified. Protein kinase C (PKC) is thought to play a central role in signal transduction in response to inflammatory stimuli. The authors studied the effect of two PKC inhibitors, staurosporine (STP) and sphingosine (SPG), on TNF prodn. in rat alveolar macrophages (AM) and in whole blood (BM) incubated with 0.25–25 000 ng/mL of LPS. The authors also assessed the role of STP encapsulation into pH-sensitive and pH-insensitive liposomes composed of cholesterol hemisuccinate/dioleoylphosphatidylethanolamine and cholesterol hemisuccinate/distearylphosphatidylcholine, resp. LPS induced a dose-dependent TNF response that was 2.5–4.5-times higher in AM than in BM with the same amt. of monocytes. SPG and STP significantly reduced TNF in both cultures by 40–96%. Encapsulation of STP into pH-sensitive, but not pH-insensitive liposomes, significantly increased the effectiveness of TNF suppression. The authors conclude that the LPS-induced TNF prodn. by AM and BM is strongly dependent on PKC activation. However, AM were less sensitive to PKC inhibition than BM.

121: **91546p Interaction of taxol and other anticancer drugs with hydroxypropyl-β-cyclodextrin.** Cserhati, Tibor; Hollo, Janos (Central Research Institute for Chemistry, Hungarian Academy of Sciences, P.O. Box 17, 1525 Budapest, Hung.). *Int. J. Pharm.* **1994,** 108(1), 69–75 (Eng). The interaction between 23 anticancer drugs and hydroxypropyl-β-cyclodextrin (HPβCD) was studied by reversed-phase charge-transfer thin-layer chromatog. and the relative strength of interaction was calcd. HPβCD formed inclusion complexes with 15 compds., the complex always being more hydrophilic than the uncomplexed drug. The inclusion forming capacity of drugs differed considerably according to their chem. structure. The intensity of interaction significantly increased with increasing hydrophobicity of the guest mol., demonstrating the preponderant role of hydrophobic interactions in inclusion complex formation.

121: **91547q Physical characteristics and dissolution kinetics of solid dispersions of ketoprofen and polyethylene glycol 6000.** Margarit, Maria Victoria; Rodriguez, Ines Carmen; Cerezo, Antonio (Department of Pharmacy and Pharmaceutical Technology, School of Pharmacy, University of Granada, Granada, Spain E-18071). *Int. J. Pharm.* **1994,** 108(2), 101–7 (Eng). The formation of solid dispersions is an effective method of increasing the dissoln. rate of poorly sol. drugs, and hence, of improving their bioavailability. The authors used the dissoln. method to prep. solid dispersions of ketoprofen and polyethylene glycol 6000 (PEG 6000), and compared the dissoln. kinetics of the dispersions with phys. mixts. and pure drug. Physicochem. characteristics were detd. by x-ray diffractometry and differential scanning calorimetry. Drug/polymer mixts. contg. up to 50% ketoprofen formed eutectic compds. The results of dissoln. kinetics studies showed that PEG 6000, when used as a carrier for solid dispersions, increased the dissoln. rate of ketoprofen. The $t_{80\%}$ of dissoln. for pure drug (88.5 min) decreased to 1.9, 4.0 and 22.5 min, resp., in solid dispersions contg. 10 : 90, 50 : 50 and 90 : 10 proportions of ketoprofen/PEG 6000. That the 10 : 90 solid dispersion displays the best dissoln. kinetics of those tested.

formulation is described in which nonionic [illegible] (niosomes) are dispersed in an aq. phase which is [illegible] an nonaq. continuous phase. The resultant vesicle [illegible] (v/w/o) system allows the delivery of vesicles in a [illegible] The formulation, stability and characteristics of [illegible] systems are described. The nonionic surfactants [illegible] vesicles (niosomes) are also employed in the [illegible] minimize surfactant redistribution. The relation [illegible] of the nonionic surfactant used for prepn. of the v/[illegible] the in vitro release of 5(6)-carboxyfluorescein (CF) [illegible] in the system was investigated, controls being water [illegible] and a vesicle suspension. A range of v/w/o systems [illegible] niosomes made from nonionic surfactants (sorbitan [illegible] 20, 40, 60 and 80) in the size range 600 nm–3.4 μm [illegible] droplets of around 5–25 μm themselves dispersed in [illegible] hexadecane, iso-Pr myristate). The in vitro release [illegible] showed a decrease in the order free soln.>vesicle [illegible] emulsion>v/w/o emulsion. The rate of release of CF [illegible] the vesicles in the v/w/o system depends on the [illegible] surfactants used. The hydrophobicity of the Span [illegible] prepn. of vesicles and the v/w/o emulsion had a significant [illegible] on the release rate. In the Span 60 formulation, the [illegible] the slowest, because Span 60 has the highest phase [illegible] and the v/w/o formulation gelled at both 25 and 37°. [illegible] the oil phase affected release as might be expected [illegible] partitioning behavior of CF. With increasing temp. [illegible] increased in Span 40 and Span 80 systems, but [illegible] the Span 60 system due to the maintenance of the gel [illegible]

121: **91549s In vitro evaluation of a series of [illegible] as dermal penetration enhancers.** Cumming, K. I.; [illegible] J. (Department of Pharmacy, The Robert Gordon [illegible] Schoolhill, Aberdeen, UK AB1 9FR). *Int. J. Pharm.* [illegible] 141–8 (Eng). The effect of a series of sodium carbo[illegible] percutaneous penetration across neonatal rat stratum [illegible] was investigated. SC was pretreated with surfactant [illegible] at the crit. micelle concn. and also at 1 mM concn. [illegible] studies were carried out on pretreated SC using flow [illegible] cells and [^{14}C]propan-2-ol as the penetrant. Enhan[illegible] were calcd. from the permeability coeff. (K_p) of the [illegible] compared to untreated controls. DSC was used to [illegible] in the lipids within the SC following pretreatment [illegible] surfactants. All the surfactant treated samples showed [illegible] K_p with a maximal effect being seen with the Cu [illegible] series. In addn., there is a good correlation between the [illegible] ratio and the decrease in lipid peak temps. as measured [illegible] The surfactants increased permeability by modifying [illegible] structure of the SC and that DSC may prove useful as a [illegible] the effects of such compds.

121: **91550k Solubility of theophylline in [illegible] methylformamide mixtures.** Gonzalez, A. Gustavo; [illegible] Angeles; Asuero, Agustin G. (Department of Analytical [illegible] University of Seville, Seville, Spain 41012). *Int. J. Pharm.* [illegible] 108(2), 149–54 (Eng). The solubilities of theophylline [illegible] H_2O–DMF mixts. were detd. and found to show [illegible] behavior. The results were treated on the basis of the [illegible] Hildebrand soly. approach, considering interaction [illegible] equation was obtained for predicting the soly. of [illegible] DMF, water and their mixts., allowing the interpolation [illegible] missing solubilities in these blends.

121: **91551m Influence of drug release rate on [illegible] absorption from polymeric ocular inserts in [illegible] rabbit.** Lee, Vincent H. L.; Li, Shao Yong; [illegible] Fabrizio Saettone, M.; Chetoni, Patrizia (School of [illegible] University of Southern California, Los Angeles, CA [illegible] *Pharmacol.* **1994,** 10(2), 421–9 (Eng). There is an [illegible] ocular inserts, regardless of the nature of the polymer, [illegible] reduce systemic drug absorption. This may not [illegible] however, since not all polymers would release drug at [illegible] and to the same extent. The objective of the present [illegible] det. how drug release rate from various polymeric [illegible] influence systemic timolol absorption in the pigmented [illegible] inserts tested were made of poly(vinyl alc.) (PVA), [illegible] cellulose (HPC), or partial Et ester of poly(vinyl [illegible] anhydride) (PVMMA), approx. 89.4% wt./wt. in all [illegible] polyvinyl alc. inserts contained timolol in salt form [illegible] 940 (PVA–C940), 8.6% wt./wt. While all inserts [illegible] timolol concn. in plasma (C_{max}), only the PVA [illegible] which released timolol rapidly in vitro, reduced [illegible] systemic timolol absorption (AUC). On the other [illegible] PVA–C940 and PVMMA inserts, which released [illegible] slowly in vitro, increased the extent of systemic [illegible] Moreover, the time at which peak timolol concn. [illegible] plasma was much delayed, raising the possibility of [illegible] absorption until discharge of the presumably [illegible] mucoadhesive solns. of PVA–C940 and PVMMA reduce [illegible] nasal cavity. Not all polymeric ocular inserts reduce [illegible] absorption. Whether an insert would do so depends on [illegible] of residence time in the conjunctival sac and rate [illegible] from the insert.

121: **91552n Pharmacokinetics of etoposide [illegible] bioerodible drug carrier implanted at [illegible]** Quigley, Henry D.; [illegible]