Experimental solubilities of budesonide, hydrocortisone, and prednisolone in ethanol + water mixtures at 298.2 K are reported. The solubility of drugs was increased with the addition of ethanol and reached the maximum values of the volume fractions of 90%, 80%, and 80% of ethanol. The Jouyban-Acree model was used to fit the experimental data, and the solubilities were reproduced using previously trained versions of the Jouyban-Acree model and the solubility data in monosolvents in which the overall mean relative deviations (OMRDs) of the models were 5.1%, 6.4%, 37.7%, and 35.9%, respectively, for the fitted model, the trained version for ethanol + water mixtures, and generally trained versions for
various organic solvents + water mixtures. Solubilities were also predicted by a previously established log-linear model of Yalkowsky with the OMRD of 53.8 %.

Title: Nanosizing and *In-vitro* Characterization of Budesonide Dispersions Prepared by Microfluidic Reactors

Authors: Hany S.M. Ali¹², Peter York¹, Nicholas Blagden¹, Amir Amani³


Address: ¹Institute of Pharmaceutical Innovation, School of Pharmacy, University of Bradford, Richmond Road, Bradford BD7 1DP, United Kingdom, ²Pharmaceutics Department, Faculty of Pharmacy, Assiut University, Egypt, ³Department of Medical Nanotechnology, School of Advanced Medical Technologies, Tehran University of Medical Sciences, Tehran, 1417614411, Iran

Budesonide, a poorly aqueous soluble steroid, is commonly used in the treatment of asthma in adults and children due to its anti-inflammatory effects. In this work a microfluidic technique was employed as a bottom-up approach to prepare nano-sized particles of budesonide. Budesonide nanodispersions were produced as a result of mixing budesonide solution in ethanol with water as antisolvent within a set of microreactors. Particle size of the produced dispersion was analyzed by photon correlation spectroscopy (PCS), while the shape of the dispersed particles was studied using transmission electron microscopy (TEM). Results of particle size analysis showed that budesonide nanodispersions (150 to
350 nm) with narrow size distributions (polydispersity index < 0.25) can be obtained. TEM showed that budesonide nano-sized particles were spherical with smooth surfaces. The impact of different factors affecting the nanoprecipitation process (drug saturation level, flow rate of drug solution and antisolvent, inlet angle of microreactors and internal diameters of microreactors) was reported. A marked effect on drug particle size was noticed with changes in flow rates of solvents and antisolvent. The in vitro aerosolization performance of one of the prepared nanodispersion was studied and compared with a commercial product of budesonide for nebulization using the Sidestream jet nebulizer. Overall results revealed that MMAD of the generated aerosol was significantly smaller (p < 0.05) than that produced the commercial microsuspension (3.9 ± 0.48 µm vs. 6.2 ± 1.09 µm, respectively). Also, a significantly higher fine particle fraction (p < 0.05) was achieved with budesonide nanodispersion versus the marketed suspension of budesonide (56.88 ± 3.37 vs. 38.04 ± 7.81, respectively).
Ketorolac tromethamine (KT) is a non-steroidal anti-inflammatory drug having a half-life of around 6 hours. This study aims to formulate sustained release forms of KT by preparing solid dispersion in the matrices of Eudragit polymers (Eud) using coevaporation technique. Two Eud polymers, namely Eud RS100 and Eud RL100, were used in preparing KT-coprecipitates at different drug:polymer ratios. The prepared KT-Eud coprecipitates were characterized for their yield, drug content and drug in vitro release patterns. In addition, physicochemical characterization was carried out on some KT-Eud coprecipitates by differential scanning calorimetry (DSC) and infrared spectroscopy (IR) to study the possibility of solid-state KT-Eud interaction. Also, KT interaction with the tested Eud polymers was carried out in solution in phosphate buffer saline (PBS, pH 7.4) along twenty days. Moreover, the analgesic activity of KT-Eud RS 100 (1:5) coprecipitate was assessed by tail-flick method and compared to that of untreated KT. The in vitro release results indicated that the dispersions made of pure Eud RS exhibited a slower release when compared to those prepared using RS/RL blends. DSC scans of KT-Eud RS 100 (1:5) systems indicated that a complete suppression of the drug fusion peaks suggesting a homogeneous dissolution of the drug in the polymer matrix. Eud RL 100 had a greater adsorptive capacity than Eud RS 100 due to the greater number of quaternary ammonium functions on RL.
surfaces. The maximum analgesic activity of KT-Eud RSR100 (1:5) coprecipitate was between 5 and 6 h extended to 10 h while the maximum analgesic activity of untreated Ketorolac was between 2 and 2.5 h.
The objective of this work was to evaluate the efficacy and suitability of different organogel formulations as transdermal delivery systems of meloxicam (MX) compared to hydrogel formulations. Hydrogels and hydroalcoholic gels were prepared using either carbopol 940 or pluronic F-127 as gelling agents. The organogels used glyceryl monostearate (GMS), a glyceryl fatty acid ester as organogelator in view of the good skin tolerability of this group of organogelators. The liquid phase was oleic acid, Myglicol 812 or Labrasol. In vitro drug release through cellophane membrane was studied. The effect of some formulation variables (organogelator concentration, type of liquid phase, drug concentration and method of drug incorporation) on the release patterns of meloxicam (MX) from different organogels was investigated. In vitro skin permeation through excised rat skin in phosphate buffer (pH 7.4) was carried out. The in vivo skin penetration was evaluated by measuring the anti-inflammatory effect in rats by the paw edema test. The highest drug release was obtained from Myglicol 812 organogel, Labrasol organogel and hydroalcoholic pluronic gel. The results revealed an inverse correlation between the drug release rate and organogelator concentration and direct correlation between the drug release rate and the initial drug concentration. The release rate of the drug was dependent on the nature of
the gel’s liquid component (which influences drug solubility), but not on the method of drug incorporation. Permeation across rat skin showed that Mygisol 812 and Labrasol organogels were superior to hydrogels and hydroalcoholic gels. The anti-inflammatory activity of the drug in different formulations was studied using carragenan-induced rat paw edema method. The results showed an excellent anti-inflammatory activity for the tested formulations, but the anti-inflammatory activity of organogels was significantly higher than that of hydroalcoholic gel. Histopathological examination of rat skin treated with the selected formulations showed normal skin histology. These findings suggest that these organogels could be effective vehicles for transdermal delivery of meloxicam.
Title: Tailoring the Efficacy of Nimodipine Drug Delivery using Nanocarriers Based on A2B Miktoarm Star Polymers

Authors: Soliman GM, Sharma R, Choi AO, Varshney SK, Winnik FM, Kakkar AK, Maysinger D

Source: Biomaterials, 32, 8382-92 (2010)
Title: Robust Polymeric Nanoparticles for the Delivery of Aminoglycoside Antibiotics Using Carboxymethyl-dextran-b-poly(ethyleneglycols) Lightly Grafted with n-Dodecyl Groups

Authors: Soliman GM, Szychowski J, Hanessian S, Winnik FM

Title: Minocycline Block Copolymer Micelles and their Anti-Inflammatory Effects on Microglia

Authors: Soliman GM, Choi AO, Maysinger D, Winnik FM

Source: *Macromolecular Bioscience, 10, 278-88 (2010)*
Title: Film Forming Gel for Treatment of Oral Mucositis: *In-vitro* Studies

Authors: Mohamed Attia, Heba Y. El Badawy

Title: Indomethacin Sustained Release Pellets Prepared by Extrusion-Spheronization

Authors: M. El-Badry, Gamal M. Mahrous, Mohamed A. Ibrahim, F.K. Al-Anazi

Title: Preparation and Investigation of Acetyl Salicylic Acid Caffeine Complex for Rectal Administration

Authors: M. El-Badry, Ehab A. Fouad, Fars K. Alanazi, Maha M. Arafah, Ibrahim A. Alsarra, Riyad Al-Ashban

Title: Design and Evaluation of Ciprofloxacin Hydrochloride Ocular Inserts

Authors: Mohamed Attia, Mohamed El Azizi, Mohamed S. Hashish

Deficiency in nutrients especially antioxidants play an important role in the pathogenesis of acquired immuno-deficiency syndrome (AIDS). Antioxidants; vitamin A, vitamin C, vitamin E, zinc and selenium are available in market as capsules. The release rate is very fast followed by fast elimination. It is necessary to prolong the residence time of antioxidants. Sustained release tablet formulation was designed and evaluated on small scale and on large scale preparations. Low attention has been discuss the use of sustained release formula in treatment of AIDS. Sustained release tablet formulation was designed and evaluated on small scale and on large scale preparations. The formulated tablets contained beta-carotene, vitamin C, tocopherol acetate, selenium, yeast and zinc pidolate. Vitamin C was chosen as tracer for detection and evaluation of tablet dosage form. Vitamin C was found to be stable in 0.1 N HCl (pH 1.2) along 8 hrs at 37°C. The formulated tablets passed the pharmacopeial requirements for all tablet
tests. The formulated tablets showed sustained release characteristics of vitamin C as a tracer, within 8 hrs.
Lornoxicam as a non-steroidal anti-inflammatory drug (NSAID) has the same side effects of this group if taken orally (GIT, renal, and hepatic disorders). Lornoxicam and its metabolites bind extensively to plasma albumin (99%), beside that, it has a relatively short half-life (3 to 5 hrs). The drug was formulated in mucoadhesive buccal patches using different polymers including, hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), hydroxypropylmethyl cellulose (HPMC), chitosan, polyvinyl alcohol (PVA), gelatin, sodium alginate and sodium carboxymethyl cellulose (Na CMC).

The physical characteristics of the formulated patches as mass uniformity, patch thickness, surface pH, folding endurance, swelling, residence time as well as mucoadhesion (in-vitro and ex-vivo mucoadhesion force) were evaluated. The in-vitro release of the drug from the formulated patches was studied using the USP dissolution apparatus, and the results indicated that HEC, HPC and chitosan showed the lowest drug release (70%, 76%, and 81%, respectively) while gelatin, sodium alginate and Na CMC gave the highest release (nearly 100%). Permeation of lornoxicam formulated in different patches through rabbit buccal mucosa was also studied and the results showed that gelatin and chitosan patches resulted in the highest drug permeation. Kinetics of drug release from the different patches was found to follow zero order or diffusion kinetics.
Title: Formulation and Characterization of Gelucire Pellets for Sustained Release of Ibuprofen

Authors: Gihan Nabil Fetih


Address: Deptartment of Pharmaceutics, Faculty of Pharmacy, Assiut University, Assiut, Egypt

The aim of the present study was to develop ibuprofen (IBU) - loaded pellets by melt solidification technique using Gelucire 50/13 (GL) as a lipid carrier in different concentrations. This system was intended to prolong the drug release in order to minimize the drug related adverse effects and improve bioavailability in different gastrointestinal tract conditions. The prepared pellets were evaluated using scanning electron microscopy (SEM), Infrared spectroscopy (IR), and Differential scanning calorimetry (DSC) studies. Process yield, drug loading, encapsulation efficiency, and particle size distribution were also investigated. The effect of agitation speed and amount of GL on pellets properties was evaluated. In-vitro drug release of ibuprofen from prepared pellets was studied in HCl buffer (pH 1.2) for 2 hrs, and in phosphate buffer (pH 7.4) for up to 8 hrs. The obtained pellets were spherical in shape with smooth surfaces; and GL showed no interaction with the drug. The release of drug from the pellets showed low percentage of drug release in pH 1.2. However, at pH 7.4 the obtained results showed that optimum levels of drug were released in a sustained manner.
Title: Design and Evaluation of Novel pH-Sensitive Chitosan Nanoparticles for Oral Insulin Delivery

Authors: Makhlof A.1,2, Tozuka Y.2, Takeuchi H.2


Address: 1Department of Industrial Pharmacy, Assiut University, Assiut, Egypt, 2Laboratory of Pharmaceutical Engineering, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan

Chitosan nanoparticles (CS NPs) have been commonly regarded as potential carriers for the mucosal delivery of therapeutic peptides because of their biocompatibility, bioadhesion and permeation enhancing properties. However, they have limited colloidal stability and readily dissociate and dissolve in the acidic gastric conditions. In the current study, CS NPs were formulated by ionic cross-linking with hydroxypropyl methylcellulose phthalate (HPMCP) as a pH-sensitive polymer and evaluated for the oral delivery of insulin. In vitro results revealed a superior acid stability of CS/HPMCP NPs with a significant control over insulin release and degradation in simulated acidic conditions with or without pepsin. Furthermore, fluorescently-labeled CS/HPMCP NPs showed a 2- to 4-fold improvement in the intestinal mucoadhesion and penetration compared to CS/TPP NPs as evidenced by quantitative fluorescence analysis and confocal microscopy. After s.c. injection to rats, no significant difference in the hypoglycemic effect of insulin solution or insulin-loaded CS/HPMCP NPs was observed, confirming the physico-chemical stability and biological activity of the entrapped peptide. Following peroral administration, CS/HPMCP NPs increased the hypoglycemic effect of insulin by more than 9.8 and 2.8 folds as compared to
oral insulin solution and insulin-loaded CS/tripolyphosphate (TPP) NPs, respectively.
Title: In-vitro and In-vivo Evaluation of WGA-Carbopol Modified Liposomes as Carriers for Oral Peptide Delivery

Authors: Makhlof A.¹,², Fujimoto S.², Tozuka Y.², Takeuchi H.²


Address: ¹Department of Industrial Pharmacy, Assiut University, Assiut, Egypt, ²Laboratory of Pharmaceutical Engineering, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan

Surface modification of liposomal nanocarriers with a novel polymer-lectin conjugate was proposed for enhancing the systemic uptake of encapsulated peptide and protein therapeutics after oral administration. Wheat germ agglutinin (WGA) was covalently attached to carbopol (CP) using the carbodiimide method. The prepared WGA-CP conjugate retained the biological cell binding activity of WGA without any evidence of cytotoxicity to Caco-2 monolayers. Cationic liposomes in the size range of 100 nm were prepared by the lipid film hydration method followed by probe sonication and surface modification with negatively charged WGA-CP. The uptake of WGA-CP liposomes by Caco-2 cells was significantly higher than non-modified or CP liposomes. The uptake was dependent on the surface concentration of WGA, temperature, and incubation period, and was significantly inhibited in the presence of chlorpromazine and 10-fold excess of free WGA. These results suggest the involvement of active transport mechanism for the cellular uptake of the modified liposomes, mediated mainly by binding of WGA to its specific cell
membrane receptors. Dual channel confocal microscopy confirmed the simultaneous association and internalization of the polymer conjugate and the liposomal carrier by Caco-2 cells and intestinal membrane of rats. In addition, the pharmacological efficacy of calcitonin, a model peptide drug, was enhanced by more than 20 and 3 folds following peroral administration of calcitonin-loaded WGA-CP liposomes as compared to non-modified and CP liposomes, respectively.
Title: A Mucoadhesive Nanoparticulate System for the Simultaneous Delivery of Macromolecules and Permeation Enhancers to the Intestinal Mucosa

Authors: Makhlof A.\(^1,2\), Werle M.\(^1\), Tozuka Y.\(^1\), Takeuchi H.\(^1\)


Address: \(^1\)Laboratory of Pharmaceutical Engineering, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan, \(^2\)Current address: Department of Industrial Pharmacy, Assiut University, Assiut, Egypt

The feasibility of combining safe permeation enhancers in a mucoadhesive particulate system for the oral delivery of peptide drugs was investigated in this study. Polyelectrolyte complex nanoparticles (NPs) were prepared by ionic interaction of spermine (SPM) with polyacrylic acid (PAA) polymer. Cytotoxicity studies in Caco-2 monolayers revealed the safety of the delivery system in the concentration range used for permeation enhancement. The cellular transport of fluorescein isothiocyanate dextran (FD4) showed higher permeation enhancing profiles of SPM-PAA NPs, as compared to SPM solution or PAA NPs prepared by ionic gelation with MgCl\(_2\) (Mg-PAA NPs). These permeation enhancing effects were associated with a reversible decrease in TEER values, suggesting a paracellular permeation pathway by reversible opening of the tight junctions. Furthermore, confocal microscopy results revealed strong association of the NPs prepared using fluorescence labeled PAA to Caco-2 cells. The permeation enhancing properties of SPM-PAA NPs were further evaluated in vivo after oral administration to rats, using FD4 and calcitonin as models of poorly permeating...
drugs. Confocal microscopy images of rats’ small intestine confirmed previous findings in Caco-2 cells and revealed a strong and prolonged penetration of FD4 from the mucosal to the basolateral side of the intestinal wall. In addition, the proposed NPs were efficient in improving the oral absorption of calcitonin, as evidenced by the significant and prolonged reduction of the blood calcemia in rats.
Title: Nanoparticles of Glycol Chitosan and its Thiolated Derivative Significantly Improved the Pulmonary Delivery of Calcitonin

Authors: Makhlof A.\textsuperscript{1,2}, Werle M.\textsuperscript{1}, Tozuka Y.\textsuperscript{1}, Takeuchi H.\textsuperscript{1}

Source: Int. J. Pharm., 397, 92-95 (2010)

Address: \textsuperscript{1}Laboratory of Pharmaceutical Engineering, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan, \textsuperscript{2}Current address: Department of Industrial Pharmacy, Assiut University, Assiut, Egypt

A novel thiomer derivative of glycol chitosan (GCS) was synthesized by coupling with thioglycolic acid (TGA) and evaluated for the pulmonary delivery of peptides. Nanoparticles (NPs) based on GCS and GCS-TGA were obtained by the ionic gelation method and demonstrated a particle size in the range of 0.23-0.33 μm with positive surface charge and high calcitonin entrapment. Fluorescent GCS-TGA NPs resulted in a 2-fold increase in mucoadhesion to lung tissue after intra-tracheal administration to rats as compared to non thiolated NPs. Evaluation of pulmonary toxicity revealed the biocompatibility of the two nanoparticulate formulations with lung tissue. The efficacy of the prepared NPs to enhance the pulmonary absorption of peptides was evaluated after pulmonary administration to rats using a liquid micro-sprayer technique. Calcitonin-loaded GCS and GCS-TGA NPs resulted in a pronounced hypocalcemic effect for at least 12 and 24 h, and a corresponding pharmacological availability of 27 and 40%, respectively. These findings suggest that both GCS and its thiomer derivative are promising and safe carriers for pulmonary peptide delivery.
Within the current study, a delivery system based on a novel polymer-lectin conjugate (carbopol-lectin) was evaluated for the oral delivery of therapeutic peptides and proteins. It was demonstrated that covalent attachment of lectin to carbopol does neither decrease nor abolish the specific binding properties of lectin. Bioadhesion studies revealed that liposomes coated with carbopol lectin are more bioadhesive than liposomes coated with unmodified carbopol. Finally, the in vivo data suggest that carbopol-lectin conjugate coated liposomes are effective oral peptide delivery systems which are capable of increasing the pharmacological effect of orally administered calcitonin.
Chemical investigation of the methanolic extract of the seeds of Cucumis melo L. var. reticulatus (Cucurbitaceae) afforded three new chromone derivatives; 5,7-dihydroxy-2-[2-(4-hydroxyphenyl)ethyl]chromone 3, 5,7-dihydroxy-2-[2-(3,4-
dihydroxyphenyl)ethyl]chromone 4, and 7-glucosyloxy-5-hydroxy-2-[2-(4-
hydroxyphenyl)ethyl]chromone 6, together with three known compounds; β-
amyrin 1, β-sitosterol 2, and β-sitosterol-3-O-β-glucopyranoside 5. Their
structures were established by UV, IR, 1D and 2D NMR, in addition to mass
spectroscopic data and comparison with literature data. The hexane and
methanolic extracts were evaluated for their antimicrobial activity, as well as
cytopotoxic activity using the brine shrimp bioassay.
Title: Methods for Preparing Heterocyclic Rings

Authors: Schofield C. J., Hamed R. B., Batchelor E. T., Ducho C.

Title: Monitoring the Activity of 2-Oxoglutarate Dependent Histone Demethylases by NMR Spectroscopy: Direct Observation of Formaldehyde

Authors: Hopkinson R. J., Hamed R. B., Rose N. R., Claridge T. D. W., Schofield C. J.

Title: Carboxymethylproline Synthase Catalysed Syntheses of Functionalised N-Heterocycles

Authors: Hamed R. B., Mecinovic J., Ducho C., Claridge T. D. W., Schofield C. J.

Title: Evidence for the Slow Reaction of Hypoxia-Inducible Factor Prolyl Hydroxylase 2 with Oxygen


Pharmacognosy

Title: Laurefurenynes A–F, new Cyclic Ether Acetogenins from a Marine Red Alga, Laurencia sp.

Authors: Wael M. Abdel-Mageed1,2, Rainer Ebel2, Fred A. Valeriote3, Marcel Jaspars2


Address: 1Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt, 2Marine Biodiscovery Centre, Department of Chemistry, University of Aberdeen, Old Aberdeen, AB24 3UE, Scotland, UK, 3Ford Cancer Center, 1 Ford Place, Detroit, M148202, USA

We report here on the discovery and structure determination of three new diastereomeric pairs of cyclic ether acetogenins, laurefurenynes A–F, isolated from the aqueous extract of the alga Laurencia sp. collected in the Philippines. Extensive use was made of NMR spectroscopic data and high resolution MS to determine the structures of the pure compounds. The most stable and the lowest energy conformation was determined using molecular modelling, and their cytotoxic activity was tested against different tumour cells, a significant indication that laurefurenyne C and F are moderately cytotoxic, but non selective whilst the others are inactive.
1 $\Delta_{3,4}^{\text{cis}}$
2 $\Delta_{3,4}^{\text{trans}}$

3 $\Delta_{3,4}^{\text{cis}}$
4 $\Delta_{3,4}^{\text{trans}}$

5 $\Delta_{3,4}^{\text{cis}}$
6 $\Delta_{3,4}^{\text{trans}}$
Dermacozines, A New Phenazine Family from Deep-Sea Dermacocci Isolated from a Mariana Trench Sediment

Authors: Wael M. Abdel-Mageed\textsuperscript{1,2}, Bruce F. Milne\textsuperscript{3}, Marcell Wagner\textsuperscript{4}, Marc Schumacher\textsuperscript{5}, Peter Sandor\textsuperscript{6}, Wasu Pathom-aree\textsuperscript{7}, Michael Goodfellow\textsuperscript{7}, Alan T. Bull\textsuperscript{8}, Koki Horikoshi\textsuperscript{9}, Rainer Ebel\textsuperscript{1}, Marc Diederich\textsuperscript{5}, Hans-Peter Fiedler\textsuperscript{4}, Marcel Jaspars\textsuperscript{1}


Address: \textsuperscript{1}Marine Biodiscovery Centre, Department of Chemistry, University of Aberdeen, Old Aberdeen, Scotland, UK AB24 3UE. E-mail: m.jaspars@abdn.ac.uk; Fax: +44 1224 272921; Tel: +44 1224 272895, \textsuperscript{2}Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt, \textsuperscript{3}Center for Computational Physics, Physics Department, University of Coimbra, Rua Larga, 3004-516, Coimbra, Portugal, \textsuperscript{4}Mikrobiologisches Institut, Universit¨at T¨ubingen Auf der Morgenstelle 28, D-72076, T¨ubingen, Germany, \textsuperscript{5}Laboratoire de Biologie Mol´eulaire et Cellulaire du Cancer, H´opital Kirchberg, 9 rue Edward Steichen, L-2540, Luxembourg, Grand-Duchy of Luxembourg, \textsuperscript{6}Varian Deutschland GmbH, Alsfelder Strasse 6, 64289 Darmstadt, Germany, \textsuperscript{7}School of Biology, University of Newcastle, Ridley Building, Newcastle upon Tyne, UK NE1 7RU, \textsuperscript{8}Department of Biosciences, University of Kent, Canterbury, Kent, UK CT2 7NJ

\textit{Dermacoccus abyssi} sp. nov., strains MT1.1 and MT1.2 are actinomycetes isolated from Mariana Trench sediment at a depth of 10 898 m. Fermentation
using ISP2 and 410 media, respectively, lead to production of seven new oxidized and reduced phenazine-type pigments, dermacozines A–G (1–7), together with the known phenazine-1-carboxylic acid (8) and phenazine-1,6-dicarboxylic acid (9). Extensive use was made of 1D and 2D-NMR data, and high resolution MS to determine the structures of the compounds. To confirm the structure of the most complex pentacyclic analogue (5) we made use of electronic structure calculations to compare experimental and theoretical UV-Vis spectra, which confirmed a novel structural class of phenazine derivatives, the dermacozines. The absolute stereochemistry of dermacoine D (4) was determined as S by a combination of CD spectroscopy and electronic structure calculations. Dermacozines F (6) and G (7) exhibited moderate cytotoxic activity against leukemia cell line K562 with IC50 values of 9 and 7 mM, respectively, while the highest radical scavenger activity was observed for dermacoine C (3) with an IC50 value of 8.4 mM.
Nature offers a huge and only partially explored variety of small molecules with potential pharmaceutical applications. Commonly used characterization methods for natural products include spectroscopic techniques such as nuclear magnetic resonance spectroscopy and mass spectrometry. In some cases, however, these techniques do not succeed in the unambiguous determination of the chemical structure of unknown compounds. To validate the usefulness of scanning probe microscopy as an adjunct to the other tools available for organic structure analysis, we used the natural product cephalandole A, which had previously been misassigned, and later corrected. Our results, corroborated by density functional theory, demonstrate that direct imaging of an organic compound with atomic-resolution force microscopy facilitates the accurate determination of its chemical structure. We anticipate that our method may be developed further towards molecular imaging with chemical sensitivity, and will become generally useful in solving certain classes of natural product structures.
SPM measurements of the unknown compound.
Title: Antimicrobial Effects of Pepper, Parsley, and Dill and their Roles in the Microbiological Quality Enhancement of Traditional Egyptian Kareish Cheese

Authors: Nahed M. Wahba¹, Amany S. Ahmed², Zedan Z. Ibraheim²


Address: ¹Animal Health Research Institute, Assiut Regional Laboratory, Assiut University, Assiut, Egypt, ²Department of Pharmacognacy, Faculty of Pharmacy, Assiut University, Assiut, Egypt

This study was designed to assess the application of some edible plants including cayenne, green pepper, parsley, and dill to Kareish cheese and to evaluate the antimicrobial activity of these plant materials against natural microflora, coliforms, molds, and Staphylococcus aureus. Twelve different concentrations of ethanol extract of the plants were prepared for determination of the minimal inhibitory concentration. Cayenne and green pepper extracts showed highest activity followed by dill and parsley against S. aureus. Addition of cayenne or green pepper to Kareish cheese during manufacture revealed that both plants were able reduce the S. aureus population to undetectable level within the first and second days of storage. To study the effect of combining plant materials on the microbiological quality of ready-to-eat Kareish cheese, the total bacterial count, coliform count, and yeast and molds counts were determined. It has been found that addition of plant materials to Kareish cheese reduced the total...
bacterial and coliform populations. All concentrations of cayenne, green pepper, dill, and parsley (9%) completely reduced the yeast count within 2 hours. Cayenne and green pepper completely reduced the mold count within 2 days, whereas parsley and dill were found to be less effective. Kareish cheese prepared with 1% cayenne pepper and 3% and 6% each of green pepper, dill, and parsley were found strongly acceptable to the consumer and considered the most preferable type. Therefore, this study revealed that pepper, parsley, and dill exhibited antibacterial activity against natural microflora, coliforms, yeast and molds, and S. aureus in Kareish cheese, and the addition of these plants is acceptable to the consumer and may contribute to the development of new and safe varieties of Kareish cheese.
Title: Constituents and Secondary Metabolite Natural Products in Fresh and Deteriorated Cassava Roots

Authors: Soad A.L. Bayoumi\textsuperscript{1,3}, Michael G. Rowan\textsuperscript{1}, John R. Beeching\textsuperscript{2}, Ian S. Blagbrough\textsuperscript{1}

Source: Phytochemistry, 71, 598-604 (2010)

Address: \textsuperscript{1}Department of Pharmacy and Pharmacology, University of Bath, Bath BA2 7AY, UK, \textsuperscript{2}Department of Biology and Biochemistry, University of Bath, Bath BA2 7AY, UK, \textsuperscript{3}Current Address: Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt

A phytochemical analysis of cassava (Manihot esculenta Crantz) fresh roots and roots suffering from post-harvest physiological deterioration (PPD) has been carried out. The first isolation and identification of galactosyl diacylglycerides from fresh cassava roots is reported as well as \(\beta\)-carotene, linamarin, and \(\beta\)-sitosterol glucopyranoside. The hydroxycoumarin scopoletin and its glucoside scopolin were identified from cassava roots during PPD, as well as trace quantities of esculetin and its glucoside esculin. There is no isoscopoletin in cassava roots during PPD.
The present state of knowledge of the phytochemistry of small molecules isolated from the roots and leaves of cassava, Manihot esculenta Crantz (Euphorbiaceae), is reviewed. Cassava roots are an important source of dietary and industrial carbohydrates, mainly eaten as a source of starch, forming the staple food to over 500 million; additionally, the roots have value as a raw material for industrial starch production and for animal feed giving the crop high economic value, but it suffers markedly from post-harvest physiological deterioration (PPD). The hydroxycoumarins scopoletin and its glucoside scopolin as well as trace quantities of esculetin and its glucoside esculin are identified from cassava roots during PPD. The biotechnological prospects for cassava are also reviewed including a critical appraisal of transgenic approaches for crop improvement, together with its use for bioethanol production, due to cassava's efficient ability to fix carbon dioxide into carbohydrate.
Title: Photoactivable Peptides for Identifying Enzyme-Substrate and Protein-Protein Interactions


Source: Chem Commun, Accepted (2010)
Pharmacognosy

Title: The 2-Oxoglutarate Dependent Oxygenase JMJD6 Catalyses Oxidation of Lysine Residues to Give 5S-Hydroxylysine Residues

Authors: Mantri M., Loik N. D., Hamed R. B., Claridge T. D. W., McCullagha J. S. O., Schofield C.J.

Source: ChemBioChem, Accepted (2010)
Title: Pentacyclic Triterpenes from *Ficus pandurata* Hance. Fruit

Authors: Amany Sayed Ahmed


Address: Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt

*From Ficus pandurata Hance fruits, six triterpenes and three sterols were isolated. The structure of these compounds were elucidated using physical and spectral characters including IR, $^1$H, $^{13}$C-NMR, including DEPT experiment and MS.*
Title: Phytochemical and Biological Study of *Eranthemum nervosum* (Vahl) R. Br., Cultivated in Egypt

Authors: Mahmoud H. Assaf¹, Yaser G. Gouda¹, Ehab S. El-Khayat², Reda A. Abd El-Hamid²


Address: ¹Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt, ²Department of Pharmacognosy, Faculty of Pharmacy, Al-Azhar University, Assiut, Egypt

Fractionation and purification of the methanolic extract of the aerial parts of *Eranthemum nervosum* (Vahl) R. Br. (Acanthaceae) cultivated in Egypt yielded eleven compounds named: \( \beta \)-amyrin (1), \( \alpha \)-amyrin (2), Lupeol (3), \( \beta \)-sitosterol (4), Apigenin (5), Kaempferol (6), \( \beta \)-sitosterol 3-O-\( \beta \)-D-glucopyranoside (7), Benzoic acid (8), Kaempferol-3-O-\( \beta \)-D-glucopyranoside (9), Syringin (10) and Apigenin 7-O-neohesperidoside (11). Identification of these compounds has been established by physical, chemical and spectral data as well as comparison with authentic samples. The LD₅₀; anti-inflammatory; antipyretic; hepatoprotective and the effect on CNS were studied.
Title: Macro- and Micromorphology of the Leaves, Stems and Flowers of *Chrysanthemum carinatum* L.

Authors: A. A. Ali, M. A. El-Shanawani, A. A. Khalifa, M. A. Mohammad


Address: Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, Egypt

The genus *Chrysanthemum* L. is sometimes called Ismelia, it comprises about 150 species native to tropical and temperate North and South America. *Chrysanthemum carinatum* L. is known as Painted daisy, German flag and Tricolor Chrysanthemum. Some species of genus *Chrysanthemum* are used medicinally to cure influenza symptoms, liver and menstrual disorders and have anti-inflammatory and antispasmodic effects.
Title: Minor Constituents from *Rubia cordifolia* L. Root

Authors: Zedan Z. Ibraheim, Yaser G. Gouda


Address: Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut, 71526, Egypt

Reinvestigation of the chloroform soluble fraction of the chloroform-methanol (1:1) extract of the dried roots of *Rubia cordifolia* L. using different chromatographic techniques led to isolation of one new naphthohydroquinone dimer (1) and four known compounds identified as 3-β-friedelinol (2), atraric acid (3), vanillic acid (4) and D-3-O-methoxy-chiro-inositol (5). The identification of the isolated compounds was carried out using different physical, chemical and spectral methods of analysis.
Synthesis and evaluation of anti-TB activity of individual compounds of Schiff bases combinatorial library were done against Mycobacterium tuberculosis H37Rv at a single concentration of 6.25 µg/mL according to the protocol of TAACF. Compounds 2C and 3D produced 99% inhibitory activity on the investigated organism, while the other tested compounds showed lower activity ranging from 35 to 84%. It was found that there are no relation between the anti-TB activity of the tested compounds and their lipophilicity expressed by C log P of these compounds. A 3D pharmacophoric model has been generated by Molecular Operating Environment (MOE) using a training set of 10 reported anti-TB compounds and testing the synthesized compounds (1A, 1B, 1D, 1E, 2C, 3A, 3C, 3D, 3E and 4A–4E). The generated pharmacophoric features include, F1: hydrogen bond donors (Don), F2: aromatic rings (Aro), F3: hydrogen bond acceptors (Acc)/metal ligator (ML), F4: Aro/hydrophobic (Hyd). In all hit set, it was found that the amidic nitrogen CONH–N=C fitted the region of the Don, F1, while the amidic carbonyl group fitted the region of the Acc/ML, F3. The distances bridging F1 to F2, F3 and F4 were essential for anti-TB activity in the developed pharmacophore model, as it was confirmed from model validation procedure.
Title: Design of Pentapeptide Inhibitors with Carboxylic Acid Bioisosteres at P1’ and P4 Positions

Authors: Harichandra D. Tagad, Yoshio Hamada, Jeffrey-Tri Nguyen, Takashi Hamada, Hamdy Abdel-Rahman, Abdellah Yamani, Ayaka Nagamine, Hayato Ikari, Naoto Igawa, Koushi Hidaka, Youhei Sohma, Tooru Kimura, Yoshiaki Kiso

Title: Synthesis and Anti-Mycobacterial Evaluation of Some Pyrazine-2-Carboxylic Acid Hydrazide Derivatives.

Authors: Mohamed Abdel-Aziz, Hamdy M. Abdel-Rahman

Source: European Journal of Medicinal Chemistry, 45 (8), 3384-3388 (2010)
The present investigation describes the synthesis; evaluation and molecular modeling studies of a series of 1-substituted-1,4-dihydropyridine-3-chloroethylurea derivatives IIIa-e as potential agents for treatment of brain tumors. The incorporation of the 1,4-dihydropyridine moiety in the structure attains an efficient site specific chemical delivery system (CDS) of the chloroethylurea (CEU) as a known antitumor pharmacophore to the brain. The target compounds IIIa-e were synthesized through reduction of the corresponding quaternary compounds IIa-e. The in-vitro oxidation studies showed that, compounds IIIa-e could be oxidized into their corresponding quaternary compounds IIa-e, respectively which attains their “locked in” characteristics as brain antitumor agents. The in-vivo studies showed that compound IIIa was able to cross the BBB at detectable concentration. In addition the in-vitro alkylating activity studies using 4-(4-nitrobenzyl)pyridine (NBP) revealed that compound IIe is an efficient alkylating agent with activity comparable to reference drug chlorambucil. The target compounds were tested for their binding to the colchicine-binding site (CBS) of β-tubulin using Molecular Operating Environment (MOE) software.
Title: Synthesis of New 4,5-3(2H)pyridazinone Derivatives and their Cardiotonic, Hypotensive, and Platelet Aggregation Inhibition Activities

Authors: Enas N. Amin¹, Abdel-Alim M. Abdel-Alim¹, Samia G. Abdel-Moty¹, Abdel-Naser A. Elshorbagi¹, Mahran Sh. Abdel-Rahman²


Address: ¹Department of Pharmaceutical Organic Chemistry, Faculty of Pharmacy and ²Department of Pharmacology, Faculty of Medicine, Assiut University, Assiut 71526, Egypt

4,5-dihydro-3(2H)pyridazinones such as CI-914, CI-930 and pimobendan along with tetrahydropyridopyridazine (endralazin) and perhydropyridazino-diazepine (cilazopril) have been used as potent positive inotropes, antihypertensives as well as platelet aggregation inhibitors. Accordingly, the present work involves the synthesis of 24 target compounds; 4,5-dihydro-3(2H)pyridazinones in addition to seven reported intermediates. The chemical structures of the new compounds were assigned by microanalysis, IR, ¹H-NMR, spectral analysis and some representatives by mass spectrometry. The positive inotropic effect of the final compounds and the intermediates (12a-12d) as well as the reported intermediate compound 10 was determined in-vitro on isolated rabbit heart in comparison to digoxin. Data obtained revealed that twelve of the test compounds exhibited higher effective response than digoxin, nine compounds elicited comparable effects to digoxin and eight compounds were less active than
digoxin. In addition, four compounds approved marked significant hypotensive effect better than that of the previously reported compound 10.

Moreover, two compounds induced complete platelet aggregation inhibition. The last two compounds were also subjected to determination of their LD₅₀ and they showed no signs of toxicity up to the dose level 300 mg/kg (i.p.), while the reported oral LD₅₀ of digoxin is 17.78 mg/kg. Correlation of cardiotonic and hypotensive activities with structures of compounds was tried and pharmacophore models were computed to get useful insight onto the essential structural features required for inhibiting phosphodiesterase-III in the heart muscles and blood vessels.
Title: Albumin-Based Nanoparticles as Magnetic Resonance Contrast Agents: I. Concept, First Syntheses and Characterisation

Authors: M. M. Stollenwerk¹, I. Pashkunova-Martic², C. Kremser³, H. Talasz⁴, G. C. Thurner³, A. A. Abdelmoez⁵,⁹, E. A. Wallnöfer³, A. Helbok⁶, E. Neuhauser⁵, N. Klammsteiner⁵, L. Klimaschewski⁸, E. Von Guggenberg⁶, E. Fröhlich⁷, B. Keppler², W. Jaschke³, P. Debbage⁵


Address: ¹Faculty of Health and Society, Malmö University, 205 06 Malmö, Sweden. ²Institute of Inorganic Chemistry, University of Vienna, Währinger Str. 42, 1090 Vienna, Austria. ³Department of Radiology, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria. ⁴Section for Clinical Biochemistry, Biozentrum of the Medical University Innsbruck, Fritz-Pregl-Straße 3, 6020 Innsbruck, Austria. ⁵Department of Anatomy, Histology and Embryology, Innsbruck Medical University, Müllerstrasse 59, 6020 Innsbruck, Austria. ⁶Department of Nuclear Medicine, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria. ⁷Center for Medical Research, Stiftungtalstrasse 24, 8010 Graz, Austria. ⁸Division of Neuroanatomy, Department of Anatomy, Histology and Embryology, Innsbruck Medical University, Müllerstrasse 59, 6020 Innsbruck, Austria. ⁹Current address: Department of Pharmaceutical Organic Chemistry, Assiut University, Assiut, Egypt
To develop a platform for molecular magnetic resonance imaging, we prepared gadolinium-bearing albumin-polylactic acid nanoparticles in the size range 20–40 nm diameter. Iterative cycles of design and testing upscaled the synthesis procedures to gram amounts for physicochemical characterisation and for pharmacokinetic testing. Morphological analyses showed that the nanoparticles were spheroidal with rough surfaces. Particle sizes were measured by direct transmission electron microscopical measurements from negatively contrasted preparations, and by use of photon correlation spectroscopy; the two methods each documented nanoparticle sizes less than 100 nm and generally 10–40 nm diameter, though with significant intrabatch and interbatch variability. The particles’ charge sufficed to hold them in suspension. HSA retained its tertiary structure in the particles. The nanoparticles were stable against turbulent flow conditions and against heat, though not against detergents. MRI imaging of liquid columns was possible at nanoparticle concentrations below 10 mg/ml. The particles were non-cytotoxic, non-thrombogenic and non-immunogenic in a range of assay systems developed for toxicity testing of nanoparticles. They were micellar prior to lyophilisation, but loosely structured aggregated masses after lyophilisation and subsequent resuspension. These nanoparticles provide a platform for further development, based on non-toxic materials of low immunogenicity already in clinical use, not expensive, and synthesized using methods which can be upscaled for industrial production.
We are developing a nanoparticulate histochemical reagent designed for histochemistry in living animals (molecular imaging), which should finally be useful in clinical imaging applications. The iterative development procedure employed involves conceptual design of the reagent, synthesis and testing of the reagent, then redesign based on data from the testing; each cycle of testing and development generates a new generation of nanoparticles, and this report
describes the synthesis and testing of the third generation. The nanoparticles are based on human serum albumin and the imaging modality selected is magnetic resonance imaging (MRI). Testing the second particle generation with newly introduced techniques revealed the presence of impurities in the final product, therefore we replaced dialysis with diafiltration. We introduced further testing methods including thin layer chromatography, arsenazo III as chromogenic assay for gadolinium, and several versions of polyacrylamide gel electrophoresis, for physicochemical characterisation of the nanoparticles and intermediate synthesis compounds. The high grade of chemical purity achieved by combined application of these methodologies allowed standardised particle sizes to be achieved (low dispersities), and accurate measurement of critical physicochemical parameters influencing particle size and imaging properties. Regression plots confirmed the high purity and standardisation. The good degree of quantitative physicochemical characterisation aided our understanding of the nanoparticles and allowed a conceptual model of them to be prepared. Toxicological screening demonstrated the extremely low toxicity of the particles. The high magnetic resonance relaxivities and enhanced mechanical stability of the particles make them an excellent platform for the further development of MRI molecular imaging.
Title: Fluorometric Study for the Reaction between Sertraline and 7-Chloro-4-nitrobenzo-2-oxa-1,3-diazole: Kinetics, Mechanism and Application for the Determination of Sertraline in Tablets

Authors: Ashraf M. Mahmoud¹, Ibrahim A. Darwish², Nasr Y. Khalil²


Address: ¹Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Egypt, ²Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

A fluorometric study has been carried out, for the first time, to investigate the reaction of the new generation antidepressant sertraline (SRT) with 7-chloro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl). In an alkaline buffered medium (pH 8.0), a green fluorescent product exhibiting maximum fluorescence intensity at 532 nm after excitation at 470 nm was produced. The factors affecting the reaction were carefully studied and the conditions were optimized. The kinetics of the reaction was investigated, the stoichiometry of the reaction was determined, and the mechanism was postulated. The activation energy of the reaction was determined and found to be 27.34 KJ mole⁻¹. Under the optimum reaction conditions, a linear relationship with good correlation coefficient (r = 0.9998, n = 6) was found between the fluorescence intensity of the reaction product and SRT concentrations in the range of 0.3–20.0 µg ml⁻¹. The limit of detection and limit of quantitation were 0.07 and 0.21 µg ml⁻¹, respectively. The intra- and inter-
assay precisions were satisfactory; the relative standard deviations did not exceed 2.61%. The proposed method was successfully applied to the determination of SRT in its pharmaceutical tablets with good accuracy; the recovery percentages were 96.97–102.23 ± 1.01–1.62%. The results were compared favorably with those of the reported method.
Title: Highly Sensitive HPLC Method with Automated Co-Sense System and Fluorescence Detection for Determination of Sertraline in Human Plasma

Authors: Nasr Y. Khalil¹, Ashraf M. Mahmoud², Ibrahim A. Darwish¹, Abdul-Rahman A. Al-Majed¹

Source: Chromatographia, 72, 825-831 (2010)

Address: ¹Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia, ²Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Egypt

A highly sensitive HPLC method with column-switching “Co-sense” system and fluorescence detection has been proposed for trace determination of sertraline (SRT) in human plasma. A simple pre-column derivatization procedure with 7-chloro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl) reagent was employed. Fluoxetine (FLX) was used as an internal standard. Plasma samples were simply deproteinated with acetonitrile and then derivatized with NBD-Cl in borate buffer of pH 7.9 at 70°C for 30 min. The derivatized samples were injected into a pretreatment column (Shim-pack MAY1-ODS) with a washing mobile phase (acetonitrile: 2% acetic acid, 40: 60) at a flow rate of 5 mL min⁻¹ for 2 min. After an automated on-line column switching (by Co-sense system) to the analytical Nucleosil C8 column (150 × 4.6 mm, 5 µm), the separation of the derivatized SRT and FLX was achieved using a mobile phase consisted of acetonitrile:10 mmol L⁻¹ sodium acetate buffer (pH 3.5):tetrahydrofuran (40:40:20, v/v) at a flow rate of
1.0 mL min\(^{-1}\). The derivatized samples were detected at emission wavelength of 531 nm after excitation at 470 nm. Under the optimum chromatographic conditions, a linear relationship with good correlation coefficient\((r = 0.9997)\) was found between the peak area ratio and SRT concentration in the range of 5 – 5000 ng mL\(^{-1}\). The limit of detection and limit of quantitation were 1.41 and 4.28 ng mL\(^{-1}\), respectively. The intra and inter-assay precisions were satisfactory; the relative standard deviations did not exceed 5.63\%. The accuracy of the method was proved; the recovery of SRT from the spiked human plasma was 99.76 - 102.62 \(\pm\) 2.19-5.63\%. The proposed method had high throughput as the analysis involved simple sample pre-treatment procedure and short run-time (~12 min). The results demonstrated that the method would have a great value if applied in bioavailability and pharmacokinetic studies for SRT.
Title: Spectral Investigation and Analytical Application of the Vinylamino-Substituted Haloquinone Derivatives of Nizatidine and Ranitidine

Authors: Ibrahim A. Darwish¹, Samiha A. Hussein², Ashraf M. Mahmoud², Ahmed I. Hassan³


Address: ¹Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia. ²Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Assiut 71526, Egypt. ³Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Al-Azhar University, Assiut, 71524, Egypt

Studies were carried out, for the first time, to investigate the formation and spectral characteristics of N-vinylamino-substituted haloquinone derivatives of nizatidine and ranitidine. The reactions involved the condensation of N-alkylvinylamine formed from the interaction between the free secondary amino groups in the investigated drugs and acetaldehyde with each of chloranil, bromanil, and 2,3-dichloronaphthoquinone. The experimental conditions affecting the reactions were optimized and the characteristics of the absorption spectra of the formed colored derivatives were established. Under the optimum reaction conditions and at the max of the formed derivatives, linear relationships were found between the absorbances and the concentrations of the investigated drugs in a concentration range of 10-250 g.ml⁻¹. The limits of assays detection were 2.1-7.77 g.ml⁻¹. The precisions of the methods were satisfactory; the relative standard deviations were 1.13-1.73%. The proposed methods were successfully applied to the analysis of the studied drugs in pure and pharmaceutical dosage forms with
good accuracy; the recovery percentages were 98.1-101.8 0.58-1.57%. The results were compared favorably with those of the official methods.
Studies were carried out, for the first time, to investigate the formation and spectral characteristics of N-vinylamino-substituted haloquinone derivatives of nizatidine and ranitidine. The reactions involved the condensation of N-alkylvinylamine formed from the interaction between the free secondary amino groups in the investigated drugs and acetaldehyde with each of chloranil, bromanil, and 2,3-dichloronaphthoquinone. The experimental conditions affecting the reactions were optimized and the characteristics of the absorption spectra of the formed colored derivatives were established. Under the optimum reaction conditions and at the $\lambda_{\text{max}}$ of the formed derivatives, linear relationships were found between the absorbances and the concentrations of the investigated drugs in a concentration range of 10–250 $\mu$g ml$^{-1}$. The limits of assays detection were 2.61–7.77 $\mu$g ml$^{-1}$. The precisions of the methods were satisfactory; the relative standard deviations were 1.13–1.73%. The proposed methods were successfully applied to the analysis of the studied drugs in pure and pharmaceutical dosage forms with good accuracy; the recovery percentages were 98.1–101.8 ± 0.58–1.57%. The results were compared favorably with those of the official methods.
Title: New Sensitive HPLC Method for Evaluation of the Pharmacokinetics of New Amantadine Prodrugs as Hepatic Delivery Systems to Enhance its Activity Against HCV

Authors: Ibrahim A. Darwish1, Tarek Aboul-Fadl1, Nasr Y. Khalil1, Ashraf M. Mahmoud2, Abdul-Rahman M. Al-Obaid1


Address: 1Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia, 2Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Egypt

To improve the efficacy of amantadine (AMD) in chronic hepatitis C therapy, various prodrugs were designed and synthesized to enhance its hepatic delivery based on the incorporation of AMD into modified bile acid or cysteine derivatives. A new sensitive and selective HPLC method with fluorescence detection has been developed and validated for determination of AMD in human plasma for evaluation of the pharmacokinetics of these prodrugs. Be- taxolol hydrochloride (BTX) was used as internal standard. AMD and BTX were isolated from plasma by protein precipitation with acetonitrile and derivatized by heating with 1,2-naphthoquinone-4-sulphonate (NQS) in alkaline medium (0.01 M NaOH) at 90±5°C for 45 min. Separations were performed in isocratic mode on Nucleosil CN column (250 mm leng 3.9 mm i.d., 5 µm particle diameter) using a mobile phase consisting of acetonitrile:10 mM sodium acetate buffer (pH 3.5):methanol (20:70:10, v/v) at a flow rate of 1.5 mL min⁻¹. The derivatized
samples were extracted with chloroform and reduced with 0.03% potassium borohydride. The reduced fluorescent AMD-NQS derivative was monitored at emission wavelength of 382 nm after excitation at 293 nm. Under the optimum chromatographic conditions, a linear relationship with good correlation coefficient ($r = 0.9989, n = 5$) was found between the peak area ratio of AMD to BTX and AMD concentration in the range of 30–3200 ng mL$^{-1}$. The limit of detection and limit of quantification were 6.7 and 21 ng mL$^{-1}$, respectively. The intra and inter-assay precisions were satisfactory; the relative standard deviations did not exceed 1.57%. The accuracy of the method was proved; the recovery of AMD from spiked human plasma were 97.51-100.95 ± 0.26-1.57%. The method had higher throughput as it involved simple sample preparation procedure and short run-time (<15 min). The results demonstrated that the proposed method would have a great value in the pharmacokinetic studies for AMD released from the synthesized produgs.
Title: Current Exposure to Persistent Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyldichloroethylene (p,p′-DDE) of Belgian Students from Food and Dust

Authors: Laurence Roosens¹, Mohamed Abou-Elwafa Abdallah²,³, Stuart Harrad², Hugo Neels¹, Adrian Covaci¹,⁴


Address: ¹Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium
²Division of Environmental Health and Risk Management, Public Health Building, School of Geography, Earth, and Environmental Sciences, University of Birmingham, Birmingham, B15 2TT, United Kingdom
³Department of Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt
⁴Laboratory for Ecophysiology, Biochemistry and Toxicology, Department of Biology, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerp, Belgium

Human exposure to individual polychlorinated biphenyl (PCB) congeners and dichloro-diphenyldichloroethylene (p,p′-DDE) through food (duplicate diets) and indoor dust ingestion was assessed for 19 Belgian students. The serum concentrations of the persistent PCB congeners in serum (PCB 118, 138, 153, 170, and 180) have been correlated with the individual intake through food and dust. Dietary intakes of ΣPCBs ranged between 40 and 204 ng/day (median...
PCB exposure through dust ingestion ranged between 0.1 and 0.8 ng/day (median 0.3) or 0.3 and 1.7 ng/day (median 0.8), assuming average dust ingestion (20 mg/day) and high dust ingestion rates (50 mg/day), respectively. Dietary intake of p,p′-DDE was comparable to that of PCBs with a range from 21 to 214 ng/day (median 92). The exposure to p,p′-DDE via dust ingestion ranged between 0.02 and 0.43 ng/day (median 0.17) or 0.05 and 1.09 ng/day (median 0.43), assuming average and high dust ingestion rates, respectively. Concentrations measured in blood serum were 28-153 ng/g lipid weight (lw) (median 74) and 32-264 ng/g lw (median 45) for ΣPCBs and p,p′-DDE, respectively. Serum concentrations in the studied population are slightly lower compared to other European populations. Inspite of the uncertainty associated with the dust ingestion rates, food was the predominant exposure pathway for each PCB congener and for p,p′-DDE in the studied population. Food intake contributed more than 99% of the combined PCB intake from food and dust. No significant positive correlations (p>0.05) were observed between the serum concentrations of PCBs and p,p′-DDE and the total intake through food and dust for each participant. Instead, it is hypothesized that past and episodic higher current intakes are more important determinants of body burden than continuous background exposures at low levels.
Title: Modification and Calibration of a Passive Air Sampler for Monitoring Vapor and Particulate Phase Brominated Flame Retardants in Indoor Air: Application to Car Interiors

Authors: Mohamed Abou-Elwafa Abdallah\textsuperscript{1,2}, Stuart Harrad\textsuperscript{1}

Source: Environmental Science and Technology, 44, 3059-3065 (2010)

Address: \textsuperscript{1}Division of Environmental Health and Risk Management, School of Geography, Earth and Environmental Sciences, University of Birmingham, Birmingham, B15 2TT, United Kingdom
\textsuperscript{2}Department of Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt

A passive air sampler was modified to monitor both vapor and particulate phase brominated flame retardants (BFRs) in indoor air using polyurethane foam disks and glass fiber filters (GFF). Significant correlation ($p<0.01$) was observed between passive (ng day$^{-1}$) and active sampler (ng m$^{-3}$) derived BFR concentrations in an office microenvironment ($r = 0.94$ and $0.89$ for vapor and particulate phase BFRs respectively). A calibration experiment was performed where concentrations of target BFRs were obtained for an office using a low volume active sampler operated over a 50 d period alongside passive samplers. The passive uptake rates of each studied BFR ranged between (0.558-1.509 ng day$^{-1}$) and (0.448-0.579 ng day$^{-1}$) for vapor and particulate phases respectively. The passive entrapment of particles by the GFF was investigated using environmental scanning electron microscopy which revealed gravitational deposition of particles as the main mechanism involved. The developed sampler was applied to monitor
BFR concentrations in 21 cars. Average concentrations of \( \Sigma \)HBCDs, TBBPA and \( \Sigma \)tetra-deca BDEs were 400, 3 and 2200 pg m\(^{-3}\) in cabins and 400, 1 and 1600 pg m\(^{-3}\) in trunks. No significant differences (p<0.05) were observed between levels of \( \Sigma \)HBCDs and \( \Sigma \)tri-to hexa- BDEs in cabins and trunks. However, TBBPA, BDE-209 and \( \Sigma \)PBDEs concentrations were significantly higher in vehicle cabins.
Title: Indoor Contamination with Hexabromocyclododecanes, Polybrominated Diphenyl Ethers, and Perfluoroalkyl Compounds: An Important Exposure Pathway for People?

Authors: Stuart Harrad¹, Cynthia A. de Wit², Mohamed Abou-Elwafa Abdallah¹,³, Caroline Bergh⁴, Justina A. Björklund², Adrian Covaci⁵, Per Ola Darnerud⁶, Jacob de Boer⁷, Miriam Diamond⁸, Sandra Huber⁹, Pim Leonards⁷, Manolis Mandalakis¹⁰, Conny Östman⁴, Line Småstuen Haug¹¹, Cathrine Thomsen¹¹, Thomas F. Webster¹²


Address: ¹Division of Environmental Health and Risk Management, School of Geography, Earth, and Environmental Sciences, University of Birmingham, Birmingham B15 2TT, U.K.
²Department of Applied Environmental Science (ITM), Stockholm University, SE-106 91 Stockholm, Sweden
³Department of Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt
⁴Department of Analytical Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden
⁵Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium
⁶National Food Administration, P.O. Box 622, SE-751 26 Uppsala, Sweden

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This review underlines the importance of indoor contamination as a pathway of human exposure to hexabromocyclododecanes (HBCDs), polybrominated diphenyl ethers (PBDEs), and perfluoroalkyl compounds (PFCs). There is ample evidence of substantial contamination of indoor dust with these chemicals and that their concentrations in indoor air exceed substantially those outdoors. Studies examining the relationship between body burden and exposure via indoor dust are inconsistent; while some indicate a link between body burdens and PBDE and HBCD exposure via dust ingestion, others find no correlation. Likewise, while concentrations in indoor dust and human tissues are both highly-skewed, this does not necessarily imply causality. Evidence suggests exposure via dust ingestion is higher for toddlers than adults. Research priorities include identifying means of reducing indoor concentrations and indoor monitoring methods that provide the most “biologically-relevant” measures of exposure as well as monitoring a wider range of microenvironment categories. Other gaps
include studies to improve understanding of: emission rates and mechanisms via which these contaminants migrate from products into indoor air and dust; relationships between indoor exposures and human body burdens; relevant physicochemical properties; the gastro-intestinal uptake by humans of these chemicals from indoor dust; and human dust ingestion rates.
Title: Selective Densitometric Determination of Four α-Aminocephalosporins Using Ninhydrin

Authors: Gamal A. Saleh, Fardous A. Mohamed, Salwa R. El-Shaboury, Azza H. Rageh


Address: Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt

A simple, selective, and precise densitometric method for analysis of four α-aminocephalosporins, namely cefaclor monohydrate, cefadroxil monohydrate, cefalexin anhydrous, and cefradine anhydrous, both in bulk drugs and in formulations was developed and validated. The method employed thin-layer chromatography (TLC) aluminium sheets precoated with silica gel G 60 F254 as the stationary phase. The solvent system consists of ethyl acetate–methanol–water with different ratios for all studied drugs (Rf values of 0.40–0.60). The separated spots were visualized as blue to violet color after spraying with ninhydrin reagent. The linear regression analysis data for the calibration plots of all studied drugs produced a good linear relationship with correlation coefficients ranging from 0.9990 to 0.9996 and coefficients of determination ranging from 0.9986 to 0.9992 over the concentration range 2–10 µg/spot. The limits of detection and quantitation for all studied drugs ranged from 0.09 to 0.23 and from 0.27 to 0.84 µg/spot, respectively. The developed method was applied successfully for the determination of the studied drugs in their pharmaceutical
dosage forms with good precision and accuracy. Also, the method can be employed as a promising stability-indicating assay.
Kinetic Spectrophotometric Determination of Certain Cephalosporins Using Iodate/Iodide Mixture

Salwa R. El-Shaboury, Fardous A. Mohamed, Gamal A. Saleh, Azza H. Rageh


Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt

A simple, precise and accurate kinetic spectrophotometric method for determination of cefradine anhydrous, cefaclor monohydrate, cefadroxil monohydrate, cefalexin anhydrous and cefixime in bulk and in pharmaceutical formulations has been developed. The method based on a kinetic investigation of the reaction of the free carboxylic acid group of the drug with a mixture of potassium iodate and potassium iodide at room temperature to form yellow coloured triiodide ions. The reaction was followed up spectrophotometrically by measuring the increase in absorbance at 352 nm as a function of time. The initial rate, fixed time, variable time and rate-constant methods were adopted for constructing the calibration curves but fixed time method has been found to be more applicable. The analytical performance of the method, in terms of accuracy and precision, was statistically validated; the results were satisfactory. The method has been successfully applied to the determination of the studied drugs in commercial pharmaceutical formulations. Statistical comparison of the results with a well established reported method showed excellent agreement and proved that there is no significant difference in the accuracy and precision.
Title: Spectrophotometric Method for Determination of Certain Cephalosporins Using 4-Chloro-7-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl)

Authors: Azza H. Rageh, Salwa R. El-Shaboury, Gamal A. Saleh, Fardous A. Mohamed

Source: Natural Science, 2 (8), 828-840 (2010)

Address: Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, 71526 Assiut, Egypt

A simple, accurate and precise spectrophotometric method has been proposed for the determination of eleven cephalosporins, namely; cefaclor monohydrate, cefadroxil monohydrate, cefalexin anhydrous, cefradine anhydrous, cefotaxime sodium, cefoperazone sodium, ceftriaxone sodium, ceftizidime pentydrate, cefazolin sodium, cefixime and cefpodoxime proxetil in bulk drug and in pharmaceutical formulations. The method depends on hydrolysis of the studied drugs using 0.5 M NaOH at 100°C and subsequent reaction of the formed sulfide ions with NBD-Cl (4-chloro-7-nitrobenzo-2-oxa-1,3-diazole) to form a yellow-colored chromogen measured at 390 nm. Different variables affecting the reaction (e.g. NaOH concentration, hydrolysis time, NBD-Cl concentration and diluting solvent) were studied and optimized. Under the optimum conditions, linear relationships with good correlation coefficients (0.9990-0.9999) were found in the range of 5-160 μg mL⁻¹ for all studied drugs. The limits of assay detection and quantitation ranged from 0.289 to 5.867 and from 0.878 to 17.778 μg mL⁻¹, respectively. The accuracy and precision of the proposed method were satisfactory. The method was successfully applied for analysis of the studied drugs in their
pharmaceutical formulations and the recovery percentages ranged from 96.6 to 103.5%.
Analytical Chemistry

Title: High-Performance Liquid Chromatographic Determination and Pharmacokinetic Study of Cefepime in Goat Plasma and Milk After Pre-Column Derivatization with Hg(I)

Authors: Nawal A. El-Rabbit¹, Hanaa M. Abdel-Wadood¹, Mohammed Sayed², Heba S. Mousa³


Address: ¹Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Assiut, Egypt. ²Department of Food Hygiene, Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt. ³Drug Research Center, Assiut University, Assiut, Egypt

A highly sensitive and selective HPLC method with UV detection was developed for the determination of cefepime in goat plasma and milk. The proposed method was based on the complexation of cefepime with Hg(I) ions that imparts the high selectivity of the proposed method with enhancement of the sensitivity which enabled the analysis of cefepime in complex matrices such as plasma and milk. Detection was performed at 263 nm, using cefuroxime sodium as an internal standard. Chromatographic separation of cefepime and the internal standard was achieved with Aqua RP-C18 column using methanol/triethylamine-acetate buffer, pH 3.5 (18:82, v/v) as mobile phase at a flow rate of 1 mL/min. Linear detector responses were observed spanning the range of 1.3–20 mg/mL. The LOD for standard cefepime was 0.43 mg/mL, whereas the LOD for cefepime in goat plasma was 0.84 mg/mL and the corresponding value in goat milk was 1.1 mg/mL. No interference from endogenous substances in plasma and milk was observed. The developed HPLC method has been successfully applied for the...
pharmacokinetic study of cefepime in goat plasma and milk for the first time, after a single intramuscular injection of 50 mg cefepime/kg body weight.
Title: The Profile of Free Amino Acids in Latent Fingerprint of Healthy and Beta-Thalassemic Volunteers

Authors: Alaa Khedr

Source: J Chromatogr. B., 878, 1576-1582 (2010)
Title: Influence of Various Concentrations of Terpene-4-ol Enhancer and Carbopol-934 Mucoadhesive Upon the In-vitro Ocular Transport and the In-vivo Intraocular Pressure Lowering Effects of Dorzolamide Ophthalmic Formulations Using Albino Rabbits

Authors: Mohsen I. Afouna, Alaa Khedr, Ashraf A. Naiem, Adnan Al-Marzoqi

Title: Kinetic Spectrophotometric Method for Determination of Ciprofloxacin and Lomefloxacin in their Pharmaceutical Formulations

Authors: Ibrahim A. Darwish, Maha A. Sultan, Hessa A. Al-Arfaj

Title: Selective Kinetic Spectrophotometric Method for Determination of Gatifloxacin Based on Formation of its N-Vinylchlorobenzoquinone Derivative

Authors: Ibrahim A. Darwish, Maha A. Sultan and Hessa A. Al-Arfaj

Title: HPTLC-Densitometric Method for Simultaneous Determination of Salmeterol Xinafoate and Fluticasone Propionate in Dry Powder Inhalers

Authors: Lantider Kasaye, Ariaya Hymete, Abdel-Maaboud I. Mohamed

Source: Accepted for publication in Vol. 18, no. 3, July (2010) of SPJ
Title: Simultaneous Determination of Candesartan Cilexetil and Hydrochlorothiazide by High-Performance Liquid Chromatography

Authors: Alaa Khedr

Title: Spectrophotometric and Spectrofluorimetric Determination of 1,4-Dihydropyridine Drugs Using Potassium Permanganate and Cerium (IV) Ammonium Sulphate

Authors: H. F. Askal¹, Osama H. Abdelmegeed², Sayed M.S. Ali², Mohamed Abo El-Hamd³


Address: ¹Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Assiut 71526, Egypt, ²Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Minia University, Minia 61519, Egypt, ³Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Al-Azhar University, Assiut 71524, Egypt

Simple and sensitive spectrophotometric and spectrofluorimetric methods have been developed for determination of 1,4-dihydropyridine (1,4-DHP) drugs based on the oxidation of the investigated 1,4-DHP drugs with acidic KMnO₄ (method I) or Ce (IV) (method II). The first method is based on the decrease in the colour of the permanganate solution due to the presence of the studied drug was measured at 525 nm. And the second method is based on monitoring the fluorescence of the produced cerium (III) at emission 355 nm (excitation at 255 nm). All variables that affect the performance of the proposed methods were carefully studied and optimized. The analytical performance of the methods was validated according to International Conference of Harmonization guidelines. The proposed methods were applied successfully to the determination of the drugs.
in commercial tablets and capsules. The results of the proposed procedures were statistically and compared with those obtained by the reference methods.