Glucosinolates, volatile constituents and biological activities of *Erysimum corinthium* Boiss. (Brassicaceae)

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Abstract

Fresh leaves, roots and ripe seeds of *Erysimum corinthium* Boiss. (Brassicaceae) were investigated to uncover their glucosinolate contents through natural autolysis and exogenous myrosinase hydrolysis. The hydrolysis products were submitted to CC-MS analysis. Six glucosinolates were identified for the first time in this plant; namely, sinigrin, progoitrin, glucoiberin, 3-(methylcarbonyl)propylglucosinolate, glucocheirolin and glucoerysolin. Glucocheirolin was the major compound accumulated in the seeds and progoitrin was the major compound in the roots, while 3-(methylcarbonyl)propylglucosinolate was the major compound in the leaves. Other volatile constituents, e.g., terpenes and fatty acids esters were also identified. Seeds and leaves showed higher antimicrobial activity than roots. Seeds showed a marked cytotoxicity in vitro against colorectal, hepatic and Hela cell lines.

Keywords: *Erysimum corinthium* – Brassicaceae – Glucosinolates – Isothiocyanates – Volatile constituents - Antimicrobial and cytotoxicity

Chromatographic Application on Calixarene Bonded Stationary Phases: A Stability Indicating LC – A Method for Determination of Celecoxib in Tablet Formulation

Hisham Hashem, Clemens Trundelberg, Thomas Jira

Abstract

A method is described for extraction and quantification of celecoxib in tablets. The extraction was achieved through centrifugation of the fine powder of the tablets in Acetonitrile (ACN). The extract was examinee] by LC. The chromatographic separation was carried out on a Caltefrontal column, a relatively new packing material consisting of silica-bonded calix[8]-arene, using isocratic binary mobile phase of ACN and H₂O (55%: 45%, v/v). A diode array detector was used at 254 nm for detection. The method was validated for system suitability, linearity, precision, limits of detection and quantitation, specificity, stability and robustness. The limits of
detection and quantitation were 0.122 and 0.488 µg/mL, respectively. The recovery value of this method was 101.88% and the reproducibility was within 2.08.

Keywords
Column liquid chromatography Calixarene columns Celecoxib

Chromatographic Application on Calixarene Bonded Stationary Phases: A Stability Indicating Method for Simultaneous Determination of Paracetamol, Caffeine and Acetylsalicylic Acid in Excedrin Tablets

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ABSTRACT
A simple, rapid and accurate, routine-LC method is described for simultaneous determination of paracetamol, caffeine and acetylsalicylic acid in a tablet formulation. This study represents a new application for the calixarene stationary phases. The chromatographic separation of the three pharmaceuticals was achieved on a Caltrex BIIIE column (250 x 4 mm, 5 µm) using a binary mobile phase of 14% ACN and 86% 50 mM NaH₂PO₄ pH 3.0 at 1 ml/min flow rate. Detection was at 214 nm. Separation was achieved in less than 1.5 min. The method was validated for system efficiency, linearity, accuracy precision, limit of detection and quantification, specificity, stability and robustness. The limits of detection were 4.88, 9.77 and 78.13 µg per 10 µL of their injected volumes, respectively. The recovery values of this method were between 94.63 and 101.85 and the reproducibility was within 3.88. The method could also be used for separation and determination of salicylic acid which is considered the most important degradation product of acetylsalicylic acid.

Keywords
Column liquid chromatography Calixarene bonded LGstationary phases Cold medicaments

Ahmed S. Zidan

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Near-Infrared Investigations of Novel Anti-HIV Tenofovir Liposomes

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ABSTRACT
Near-infrared (NIR) approaches is considered one of the most well-studied process analyzers evolving from the process analytical technology initiatives. The objective of this study was to evaluate NIR spectroscopy and imaging to assess individual components within a novel tenofovir liposomal formulation. By varying stearylamine, as a positive charge imparting agent, five batches were prepared by the thin film method. Each formulation was characterized in terms of drug entrapment efficiency, release characteristics, particle sizing, and zeta potential. Drug excipients compatibility was tested using Fourier transform infrared spectroscopy, differential scanning calorimetry, and X-ray diffraction. The obtained results showed an increase in drug entrapment and a slower drug release by increasing the incorporated percentage of stearylamine. The compatibility testing revealed a significant interaction between the drug and some of the investigated excipients. The developed NIR calibration model was able to assess drug, phospholipid, and stearylamine levels along the batches. The calibration and prediction plots were linear with correlation coefficients of more than 0.9. The root square standard errors of calibration and prediction did not attain 5% of the measured values confirming the accuracy of the model. In contrast, NIR spectral imaging was capable of clearly distinguishing the different batches, both qualitatively and quantitatively. A linear relationship was obtained correlating the actual drug entrapped and the predicted values obtained from the partial least squares images.

**KEY WORDS:** characterization; chemical imaging; liposomes; near infrared; tenofovir.

**Formulation and Evaluation of a Protein-Loaded Solid Dispersions**

**By Non-Destructive Methods**

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**ABSTRACT**

The purpose of this investigation was to develop solid dispersion (SD) formulation of cyclosporine (CyA) using polyethylene glycol (PEG-6000) to enhance its dissolution rate followed by nondestructive method for the prediction of both drug and carrier. SD formulations were prepared by varying the ratio of CyA and PEG-6000 by solvent evaporation technique and characterized by dissolution, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), Fourier transform infrared (FTIR), powder X-ray diffraction (PXRD), near infrared (NIR) and near infrared chemical imaging (NIR-Cl). Dissolution data revealed enhanced dissolution of CyA when compared with pure CyA. DSC results showed that the crystallinity of PEG-6000 has decreased as indicated by decrease in the enthalpy of fusion and melting peak in the formulations. FTIR data demonstrated no chemical interaction between drug and carrier. The surface morphology of SD formulations was similar to PEG-6000 particle. NIR-Cl disclosed homogeneity of SD matrix as indicated by symmetrical histograms with smaller values of skewness. Similar to NIR, a multivariate peak
evaluation with principal component analysis and partial least square (PLS) were carried out with PXRD spectral data. PLS models with both techniques showed good correlation coefficient and smaller value of root mean square of errors. The accuracy of model for predicting CyA and PEG-6000 in NIR and PXRD data were 5.22%, 5.35%, 5.27%, and 2.10%, respectively. In summary, chemometric applications of nondestructive method sensors provided a valuable means of characterization and estimation of drug and carrier in the novel formulations.

**KEY WORDS:** cyclosporin; NIR; PEG-6000; PXRD; solid dispersion.

The AAPS journal, 2010  
**Online Monitoring of PLGA Microparticles Formation Using Lasentec Focused Beam Reflectance (FBRM) and Particle Video Microscope (PVM)**

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**ABSTRACT.**
Knowledge of the effects of different product and process variability on microparticle characterization is essential for the successful development, optimization, and scale-up of an encapsulation process. In the current research, the qualitative application of the Lasentec focused beam reflectance (FBRM) system for online monitoring of microparticle size distribution was demonstrated, Lasentec particle vision and measurement (PVM) images were also employed to follow up the steps of microparticle formation and ripening. The drug entrapment efficiency and drug release characteristics were found to be dependent on the polymer, drug, and surfactant concentrations. DSC, FTIR, and XRD data revealed that the drug was compatible with the matrix forming polymer in the solid state. As indicated from the chord count data, FBRM was sensitive to the amount of the solid materials and the number of microparticles formed. Linear relationships with good correlations were obtained between polymer, drug, and surfactant levels and the disappearance rate of 5 to 36.8, 18.4 to 135.9, and 63 to 398 urn chord length fractions. Upon organic solvent evaporation, PVM imaging detected various stages of microemulsion droplets, sheath formation, and solidification with subsequent microparticle hardening. This study illustrated the utility of FBRM and PVM in monitoring the progress of particle formation during drug encapsulation.

**KEY WORDS:** biodegradable polymers; FBRM and PVM; Lasentec; microparticles; particle sizing.

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**QbD approach of rapid disintegrating tablets incorporating indomethacin solid dispersion**
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ABSTRACT

The development of rapid disintegrating tablets (RDT) requires the use of highly soluble components to support the intended use of these products. In an attempt to prepare RDT of indomethacin, its solid dispersion with polyvinyl pyrrolidone K25 (PVP) was incorporated in a fast disintegrating matrix. Drug polymer interactions were investigated using X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FTIR). Indomethacin 1:1 solid dispersion with PVP was used to prepare its RDT. Two factors at 3 levels full factorial design were employed as a statistical approach to optimize the amount of superdisintegrant (Ac-di-sol) and hardness value regarding the desired disintegration and release characteristics. Drug to carrier ratio was the controlling factor for dissolution improvement. XRD and FTIR data revealed a remarkable interaction between the drug and the carrier that might be responsible for the dissolution enhancement. Multiple regression analysis revealed a significant effect of the polynomial terms for obtaining rapid disintegrating tablets. It was inferred that the hardness value is the most important factor controlling the disintegration time and the release characteristics. In conclusion, this study demonstrated that quality by design (QbD) is a potential paradigm for understanding the quality and optimizing the formulation of RDT containing indomethacin solid dispersion.

Keywords: Indomethacin; polyvinyl pyrrolidone; solid dispersion; rapid disintegrating tablets; factorial design


Understanding the quality of protein loaded PLGA nanoparticles variability by Plackett-Burman design

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ABSTRACT

The aim of this investigation was to screen and understand the product variability due to important factors affecting the characteristics CyA-PLGA nanoparticles prepared by 0/W emulsification-solvent evaporation method. Independent variables studied were cyclosporine A (CyA) (X1), PLGA (X2), and emulsifier concentration namely SLS (X3), stirring rate (X4), type of organic solvent employed (chloroform or
dichloromethane, $X_3$) and organic to aqueous phase ratio ($X_6$). The nanoparticles properties considered were encapsulation efficiency ($Y_1$), mean particle size ($Y_2$), zeta potential ($Y_3$), burst effect ($Y_4$) and dissolution efficiency ($Y_5$). The statistical analysis of the results allowed determining the most influent factors. The nanoparticles were characterized by scanning electron microscopy (SEM), differential scanning calorimetry (DSC), X-ray powder diffraction (XRD) and Fourier transform infrared (FTIR) spectroscopy. The factors combination showed variability of entrapment efficiency ($Y_1$), mean particle size ($Y_2$) and zeta potential ($Y_3$) from 10.17% to 93.01%, 41.60 to 372.80 nm and 29.60 to 34.90 mV, respectively. Initially, nanoparticles showed burst effect followed by sustained release during the 7-day in vitro release study period. The dissolution efficiency ($Y_5$) varied from 52.67% to 84.11%. The nanoparticles revealed Higuchi release pattern and release occurred by coupling of diffusion and erosion. In conclusion, this study revealed the potential of QbD in understanding the effect of formulation and process variables on the characteristics on CyA-PLGA nanoparticles.

Keywords: CyA, PLGA, QbD, Plackett-Burman, Nanoparticles and dissolution efficiency

International J. of Pharmaceutics, 2010

Rank: B

Tablet splitting: Product quality assessment of metoprolol succinate extended release tablets

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ABSTRACT

Metoprolol succinate extended release tablets comprise a multiple unit system containing metoprolol succinate in a multitude of controlled release pellets. Each pellet acts as a separate drug delivery unit and is designed to deliver metoprolol continuously over the dosage interval. Despite the flexibility that controlled release pellets may offer, segregation is one of the challenges that commonly occur during tableting for such drug delivery system. Since all commercial metoprolol succinate extended release tablets are scored, they are deemed suitable for splitting. The present study was aimed at utilizing an innovative technology to determine the dose uniformity for split tablets. Four marketed drug products consisting of innovator and generics were evaluated for effect of splitting on weight, assay and content uniformity. Novel analytical tool such as near infrared (NIR) chemical imaging was used to visualize the distribution of metoprolol succinate and functional excipients on the surfaces of the marketed tablets. The non-homogeneous distribution of directly compressed metoprolol succinate beads on the surface of the tablets as well as the split intersection explained the large variation in the split tablets' weight and content uniformity results. The obtained results indicated the usefulness of NIR chemical imaging to determine the need for content uniformity studies for certain split tablets.

Keywords: Tablet splitting Quality assessment Near infrared mapping
Osama I. El-Sabbagh

Arch. Pharm. Chem. Life Sci. 2010, 9, 519-527

Rank: B

Synthesis of New Nonclassical Acridines, Quinolines, and Quinazolines Derived from Dimedone for Biological Evaluation

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New nonclassical acridines, quinolines, and quinazolines were prepared starting from cyclic fi-diketoncs, namely dimedone, through application of Hantzsch addition, Michael addition, and Mannich reactions, respectively. The antimicrobial activity revealed that decahydroacridin-1,8-dione 2e bearing a 3-nitrophenyl group and hexahydroquinoline 4e having a 2,4-dichlorophenyl moiety were the most active compounds against both Gram-positive and -negative bacteria based upon using the disc diffusion method. Cytotoxic activity studies for decahydroacridin-1,8-diones 2a-e against liver carcinoma cells (IiepG2) using the MTT cell viability assay revealed that decahydroacridin-1,8-dione bearing a 4-methylphenyl moiety 2d showed a higher cytotoxic activity (IC₅₀ = 4.42) than the other derivatives.

Keywords: Acridines / Antimicrobial / Cytotoxic activity / Quinolines / Quinazolines


Rank: B

Synthesis of New 2,3-Dihydroquinazolin-4(1 H)-one Derivatives for Analgesic and Anti-inflammatory Evaluation

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Starting from isatoic anhydrides, several new 2,3-dihydroquinazolin-4(IH)-one derivatives bearing chalcone or pyrazole or thiazole moieties at the third position were synthesized. The analgesic and anti-inflammatory activities for most compounds were studied at a dose level of 50 mg/ kg via the acetic-acid-induced writhing-response method and carrageenan-induced edema method, respectively. The study showed that the chalcones bearing a 4-chlorophenyl group 4c or 4-nitrophenyl group 4b were the most active ones as analgesics. Both chalcone 4c and N-phenyl pyrazole bearing 4-methoxy phenyl group 5b showed a higher anti-inflammatory activity than cdecoxib but still lower than that of diclofenac sodium. Moreover, the chalcone 4c has nearly the same ulcerogenic index as the selective cyclooxygenase-2 inhibitor celecoxib.

Keywords: Analgesic activities Anti-inflammatory activities / Dihydroquinazolinone Synthesis
New octahydroquinazoline derivatives: Synthesis and hypertensive activity

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ABSTRACT
Several novel 1-(4-chlorophenyl)-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydro-5-oxo-3-(substitutedphenyl) quinazoline derivatives (2—21) structurally similar to prazosin, were prepared using Mannich reaction of 3-(4-chlorophenylamino)-5,5-dimethyl-2-cyclohexenone (1) with different aromatic amines in the presence of formaline. The structures of the quinazoline derivatives were established using elemental and spectral analyses. Compounds 18, 20 and 21 were found to possess a high hypertensive effect through their expected $\alpha_1$-blocking activity like the clinically used drug prazosin but with advantageous of being did not cause reflex tachycardia and having prolonged duration of action when tested in adrenaline-induced hypertension in anaesthetized rats.

Keywords: Synthesis, Octahydroquinazoline derivatives, Hypotensive activity

Mervat E. Asker

Effect of prolonged intake of iron enriched diet on testicular functions of experimental rats

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ABSTRACT
Iron deficiency anemia represents a common nutritional problem which affects many societies allover the world and iron fortified diet has been suggested as one of possible tools to combat and solve such problem. Present study was designed to illustrate the effect of dietary iron intake on certain biochemical markers dealing with oxidative stress, inflammatory response and cellular alterations of testicular tissues. Adult male rats which were fed on biscuits fortified with iron (0.3% ferrous sulfate) daily for 10 weeks (iron group) showed increased serum iron, ferritin, tumor necrosis factor-alpha (TNF-$\alpha$), nitric oxide (NO) and decreased Testosterone level (p < 0.05). Testicular tissues content of Malondialdehyde (MDA), hydroxypro-line (Hyp), iron showed significant increase (p < 0.05) and decreased glutathione (GSH) as compared to control group. Testicular tissues demonstrated massive iron distribution in sertolinterstitial tissues and degeneration of germinal epithelial cells. Apparent reduction in number of sperms and spermatogenic cells were also observed. These
symptoms may demonstrate that prolonged intake of Biscuit fortified with iron causes certain testicular damage through certain mechanism.

Keywords: Iron Overload; Oxidative Stress; Inflammatory Response of Rat Testis

Abdalla Shalaby

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Rank: B

Construction and Optimization of Selective Membrane Electrodes for Determination of Doxepin Hydrochloride in Pharmaceutical Preparations and Biological Fluids

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ABSTRACT
The construction and performance characteristics of doxepin hydrochloride selective electrodes were developed. Three types of electrodes: plastic membrane I, coated wire II, and coated graphite rod III were constructed based on the incorporation of doxepin hydrochloride with ammonium reineckate. The influence of membrane composition, kind of plasticizer, pH of the test solution, soaking time, and foreign ions on the electrodes was investigated. The electrodes showed a Nernstian response with a mean slope of 57.41 ± 0.5, 56.22 ± 0.2 and 52.88 ± 0.7 mV at 25 °C for electrode I, II and III respectively, over Doxepin hydrochloride concentration range from 1 x 10⁻² to 1 x 10⁻⁶ M, 5 x 10⁻² to 1 x 10⁻⁶ M and 1 x 10⁻³ to 5 x 10⁻⁶ M, and with a detection limit 5.0 x 10⁻⁷ M, 6.3 x 10⁻⁷ M and 2.5 x 10⁻⁶ M for electrode I, II and III respectively. The constructed electrodes gave average selective precise and usable within the pH range 3-7. Interferences from common cations, alkaloids, sugars, amino acids and drug excipients were reported. The results obtained by the proposed electrodes were also applied successfully to the determination of the drug in pharmaceutical preparations and biological fluids.

Keywords: Plastic membrane, Coated wire electrode, Coated graphite rod, Ion-selective electrode, Doxepin hydrochloride

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Rank: D

Development of tetrazepam-selective membrane sensors and their applications in Pharmaceutical preparations and biological fluids

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ABSTRACT
The construction and performance characteristics of tetrazepam selective electrodes were developed. Two types of electrodes: plastic membrane I and coated wire II were constructed based on the incorporation of tetrazepam with phosphomolybdic acid. The
influence of membrane composition, kind of plasticizer, pH of the test solution, soaking time, and foreign ions on the electrodes were investigated. The electrodes showed a Nernstian response with a mean calibration graph slope of $58.88 \pm 0.5$ and $59.18 \pm 0.1$ mV decade$^{-1}$ at $25^\circ$C for electrode I and II respectively, over tetrazepam concentration range from $5 \times 10^{-3}$-1 $\times 10^{-6}$M and $1 \times 10^{-2}$-1 $\times 10^{-6}$M and with detection limit $5.0 \times 10^{-7}$M and $4.8 \times 10^{-7}$M for electrode I and II respectively. The constructed electrodes gave average selective precise and usable within the pH range 4-6. Interferences from common cations, alkaloids, sugars, amino acids and drug excipients were reported. The results obtained by the proposed electrodes were also applied successfully to the determination of the drug in pharmaceutical preparations and biological fluids.

**Keywords:** Plastic membrane; Coated wire electrode; Ion-selective electrode; Tetrazepam; Potentiometric determination.

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**Development and validation of a HPLC method for the determination of voriconazole and its degradation products in pharmaceutical formulation**

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**ABSTRACT**

Simple, sensitive and accurate stability indicating analytical method for voriconazole has been developed and validated by using RP-HPLC techniques and applying the proposed method in the assay of voriconazole tablets (Vfend®), since there is no official monograph. The procedure was developed and validated under acidic, basic, oxidative and photo-irradiated conditions. Chromatography was performed with mobile phase containing a mixture of acetonitrile and 0.05M disodium hydrogen phosphate buffer, pH 5.5 (1:1, v/v) with flow rate of 1.0 ml per min., Cjs column and UV detection at 255 nm. developed method satisfies the system suitability criteria, peak integrity, and resolution for the parent drug and its degradants. The method was validated for linearity (correlation coefficient = 0.9999), accuracy, robustness and precision. The proposed method was simple, highly sensitive, precise and accurate and the run time less than 15 minutes indicating that the method is useful for routine quality control analysis and stability testing. Voriconazole was determined to be more sensitive to the basic conditions, photodegradation is observed only under severe conditions of light exposure, oxidation may also appear, but it was stable in acidic medium.

**Keywords:** Assay, stability indicating method, voriconazole, HPLC.
Construction of different types of ion-selective electrodes and validation of direct potentiometric determination of phenytoin sodium

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ABSTRACT
The construction and performance characteristics of phenytoin sodium selective electrodes are detailed. Two types of electrodes: plastic membrane I and coated wire II, were constructed based on the incorporation of phenytoin sodium with tungstosilicic acid. The influence of membrane composition, kind of plasticizer, pH of the test solution, soaking time and the electrodes' foreign ions were investigated. The electrodes showed a Nernstian response with a mean calibration graph slope of 30.9 ± 0.1 and 28.9 ± 0.1 mV decade⁻¹ at 25°C for electrode I and II respectively, over a phenytoin sodium concentration range of 5 × 10⁻³ - 5 × 10⁻⁶ M and 1 × 10⁻³ - 1 × 10⁻⁶ M with a detection limit 1.3 × 10⁻⁹ M and 2.5 × 10⁻⁷ M for electrode I and II, respectively. The electrodes gave average selective precision and were usable within the pH range 6-10. Interference studies from communications, alkaloids, sugars, amino acids and drug excipients are reported. The results obtained by the proposed electrodes were also applied successfully for the determination of the drug in pharmaceutical preparations and biological fluids.

Keywords: Plastic membrane • Coated wire electrode • Ion-selective electrode • Phenytoin sodium • Potentiometric titration

Hanan M. El-Nahas
Pharm. Sci. &Res. 2010, 2 (10), 663-671

Optimization of Eudragit RS Microspheres for controlled release of Theophylline using Response Surface Methodology

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ABSTRACT
The present study reports on the production of theophylline loaded Eudragit RS microspheres for controlled release. The microspheres were prepared by the emulsion solvent evaporation technique using Eudragit RS as the polymer. A three-factor, three-level design of experiment (DOE) with response surface methodology (RSM) was run to evaluate the main and interaction effect of several independent formulation variables that included theophylline concentration (X₁), stirring rate (X₂) span 80 concentration w/w (X₃). The dependent variables included encapsulation efficiency (Y₁) and cumulative percent release at 6hrs (Y₂). A desirability function was used to maximize encapsulation efficiency and to obtain controlled release formula. The drug concentration had a positive effect on the encapsulation efficiency and a negative effect on cumulative recent release, stirring rate and span concentration had a positive
effect on the cumulative recent release and a negative effect on encapsulation efficiency. Drug-loaded microspheres were spherical in shape and had a smooth surface with encapsulation efficiency ranging between 26.48 - 51.41%. Cumulative percent release were 39 - 69% for the 6hrs under most of the operating parameters studied.

Mohamed M. El-Seweidy

Inter. Journal of Biology and Biomedical Engineering, 2010, 1

Rank: C

Pattern of gastritis as manipulated by current state of Helicobacter pylori infection


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ABSTRACT

Helicobacter pylori (H. pylori) infection prevails from 60-80% in patients with gastric ulcer and 90-100% in those having duodenal ulcer. Patients with such type of chronic infection are at increased risk to develop peptic ulcers or gastric adenocarcinomas. The present work aims mainly to identify the pattern of chronic gastritis and potential effect of H. pylori infection using certain biomarkers, histological and immunochemical tests.

Fifty eight individuals, clinically diagnosed as having chronic gastritis, were participated in the present study. They were categorized into 2 groups, the first one (31%) demonstrated positive reaction to IgM antibodies of Helicobacter pylori (H. pylori) (>40u/ml) and the second group (69%) demonstrated negative reaction. Blood and antral biopsy samples were collected, directed to determination of serum gastrin, pepsinogen I (PgI), pepsinogen II (PgII), prostaglandin E-2 (PGE(2)) and interleukin-6 (IL-6). Immunohistochemistry technique was also done in antral biopsy to demonstrate the expression of inducible nitric oxide synthase (iNOS), nitrotyrosine, DNA fragmentation, myeloperoxidase and histopathological examination.

Serum gastrin, PgI, PgII, PGE(2), IL-6 demonstrated significant increase in gastritis patients as compared to normal group. PgI, PgII showed significant increase joined with slight increase of IL-6 in IgM positive group as compared to negative one. Immunostaining testes in antral biopsy showed strong positive reactions for the above mentioned markers as compared to IgM negative group (mild positive reaction).

In conclusion, gastritis patients who express IgM antibodies for H. pylori infection showed higher gastrinaemia and more pronounced atrophic, inflammatory and apoptotic damage than those not expressing IgM antibodies.
Small-dense LDL and LDL glycation in metabolic syndrome and in statin-treated and non-statin-treated type 2 diabetes

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ABSTRACT
Small-dense LDL (SD-LDL) has been particularly implicated in atherosclerosis. It has previously been reported that in non-diabetic people SD-LDL is preferentially glycated. The distribution of glycatedapolipoprotein B (glyc-apoB) in lipoproteins in metabolic syndrome (MS) and in type 2 diabetes has not previously been studied. Plasma apoB and glyc-apoB were determined in different apoB-containing lipoproteins including buoyant and SD-LDL in MS (n=18) and type 2 diabetes (DM) [n=48; 12 statin-untreated (DM-S) and 36 statin-treated (DM+S)]. Plasma glyc-apoB was 5.6 ± 0.9, 3.5 ± 0.5 and 4.0 ± 0.2 mg/dl in DM-S, DM+S and MS, respectively. The glycated proportion of SD-LDL-apoB was greater than buoyant LDL in all groups. SD-LDL contributed most to plasma glyc-apoB in DM-S, because SD-LDL-apoB was higher in DM-S than in MS and DM+S (p < 0.001). Plasma glyc-apoB correlated with SD-LDL-apoB (r=0.74, p < 0.0001 in diabetes and r=0.53, p< 0.001 in MS), but not with HbA₁c. SD-LDL is preferentially glycated in type 2 diabetes and MS. Its concentration is a stronger determinant of plasma glyc-apoB than glycaemia. Statin-induced changes in its level may be important in decreasing apoBglycation in diabetes. These findings may explain the small effect of improving glycaemia relative to statin treatment in reducing atherosclerosis risk in type 2 diabetes and the increased risk in MS even before the onset of type 2 diabetes.

Key words
Glycaemic control, glycation, metabolic syndrome, small-dense LDL, statin, type 2 diabetes

Gamal H. Ragab

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Application of non-steroidal anti-inflammatory drugs for palladium determination

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A highly sensitive spectrophotometric method for palladium determination vising piroxicam and tenoxicam as new chromogenic reagents has been developed. In the presence of sodium lauryl sul-fate (SLS), palladium reacts with piroxicam (PX) or tenoxicam (TX) to form stable yellow orange complexes in an acetate buffer solution
of pH 5.0 at 424 nm and 426 nm with molar absorptivity of $7.16 \times 10^4$ L mol$^{-1}$ cm$^{-1}$ and $1.20 \times 10^5$ L mol$^{-1}$ cm$^{-1}$, respectively. Sandell sensitivity, detection, and quantitation limits were also calculated. Optimum conditions were evaluated considering pH, reagent concentration, time, temperature, and surfactant concentration. The complex system conforms to Beer's law over the range of 0.07-1.28 µg mL$^{-1}$ palladium. The stoichiometric ratio and stability constant were also evaluated. Tolerance limits of many cations and anions were determined. Finally, the proposed method was applied successfully in the determination of palladium in jewellery, anode mud, synthetic mixtures, catalysts, and alloy samples.

**Keywords:** palladium complexes, spectrophotometry, industrial analysis, non-steroidal anti-inflammatory compounds

Mohamed I. Hussein

Molecular Microbiology, 587-604

**The high affinity iron permease is a key virulence factor required for Rhizopusoryzaepathogenesis**

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**SUMMARY**

*Hhizopusoryzaeis* is the most common cause of mucormycosis, an angiomvasive fungal infection that causes more than 50% mortality rate despite first-sline therapy. Clinical and animal model data clearly demonstrate that the presence of elevated available serum iron predisposes the host to mucormycosis. The high affinity iron permease gene (*FTR1*) is required for *R. oryzae* iron transport in iron-depleted environments. Here we demonstrate that *FTR1* is required for full virulence of *R. oryzae* in mice. We show that *FTR1* is expressed during infection in diabetic ketoacidosis (OKA) mice, in addition, we disrupted *FTR1* by double cross-over homologous recombination, but multinucleated *R. oryzae* could not be forced to segregate to a homokaryotic null allele. Nevertheless, a reduction of the relative copy number of *FTR1* and inhibition of *FTR1* expression by RNAi compromised the ability of *R. oryzae* to acquire iron in vitro and reduced its virulence in OKA mice. Importantly, passive immunization with anti-Ftrlp immune sera protected DKA mice from infection with *R. oryzae*. Thus, *FTR1* is a virulence factor for *R. oryzae*, and anti-Ftrlp passive immunotherapy deserves further evaluation as a strategy to improve outcomes of deadly mucormycosis.

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Novel cancer vaccine based on genes of *Salmonella* pathogenicity island 2

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Although tumors express potentially immunogenic tumor-associated antigens (TAAs), cancer vaccines often fail because of inadequate antigen delivery and/or insufficient activation of innate immunity. Engineering nonpathogenic bacterial vectors to deliver TAA of choice may provide an efficient way of presenting TAAs in an immunogenic form. In this study, we used genes of *Salmonella* pathogenicity island 2 (SPI2) to construct a novel cancer vaccine in which a TAA, survivin, was fused to SseF effector orotein and placed under control of SsrB, the central regulator of SPI2 gene expression. This construct uses the type III secretion system (T3SS) of *Salmonella* and allows preferential delivery of tumor antigen into the cytosol of antigen-presenting cells for optimal immunogenicity. In a screen of a panel of attenuated strains of *Salmonella*, we found that a double attenuated strain of *Salmonella typhimurium*, MvP/28 (purD/htrA), was not toxic to mice and effectively expressed and translocated survivin protein inside the cytosol of murine macrophages. We also found that a ligand for CDId-reactive natural killer T (NKT) cells, oc-glucuronosylceramide (GSL1), enhanced MvP728-induced interleukin-12 production in human dendritic cells and that in vivo coadministration of a NKT ligand with MvP728-Llo or MvP728-survivin enhanced effector-memory cytotoxic T lymphocyte (CTL) responses. Furthermore, combined use of MvP728-survivin with GSL1 produced antitumor activity in mouse models of CT26 colon carcinoma and orthotopic DBT glioblastoma. Therefore, the use of TAA delivery via SPI-2-regulated T3SS of *Salmonella* and NKT ligands as adjuvants may provide a foundation for new cancer vaccines.

Infection and immunity, 4828-4838

Efficacy of Intracellular Activated Promoters for Generation of *Salmonella*-Based Vaccines

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*Salmonella enterica* is a versatile vaccine carrier for heterologous antigens. One strategy for vaccine antigen delivery is the use of live attenuated *S. enterica* strains that translocate heterologous antigens into antigen-presenting cells by means of type
HI secretion systems (T3SS). The feasibility of this approach has been demonstrated in various experimental vaccination studies. The efficacy of recombinant live vaccines is critically influenced by the optimal level of attenuation and many other factors. For the rational design of approaches involving translocation by T3SS, additional parameters are the level of expression of the heterologous antigens and the selection of carrier proteins for the delivery of antigens to desirable subcellular compartments of the target cell. We deployed the *Salmonella* pathogenicity island 2 (SP12)-encoded T3SS for antigen delivery. The SPI2-T3SS and effector proteins are encoded by members of the large SsrAB regulon, including promoters with highly variable strength of expression. We investigated the effect of various *in vivo* activated promoters of the SsrAB regulon on the efficacy of recombinant *Salmonella* vaccines. We observed that the use of promoters with higher strength results in greater synthesis of recombinant antigens and greater stimulation of T-cell responses in cell culture assays for the stimulation of T cells by the model antigen ovalbumin. In contrast, in vaccination experiments, promoters with a low level of expression resulted in the induction of higher amounts of T cells reactive to the model antigen *Ustilolisum*. These results demonstrate that high-level expression of heterologous antigens does not necessarily result in optimal stimulation of immune responses.

**Maged E. Mohamed**

The plant cell 2010

**Arachidonic Acids: An Evolutionary Conserved Signaling Molecule Modulates Plant Stress Signaling Networks**

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Fatty acid structure affects cellular activities through changes in membrane lipid composition and the generation of a diversity of bioactive derivatives. Eicosapolyenoic acids are released into plants upon infection by oomycete pathogens, suggesting they may elicit plant defenses. We exploited transgenic *Arabidopsis thaliana* plants (designated EP) producing eicosadienoic, cicosatrienoic, and arachidonic acid (AA), aimed at mimicking pathogen release of these compounds. We also examined their effect on biotic stress resistance by challenging EP plants with fungal, oomycete, and pathogens and an insect pest. EP plants exhibited enhanced resistance to all biotic challenges, except they were susceptible to bacteria than the wild type. Levels of jasmonic acid (JA) were elevated and levels of salicylic acid
were reduced in EP plants. Altered expression of JA and SA pathway genes in EP plants shows that eicosapolyenoic effectively modulate stress-responsive transcriptional networks. Exogenous application of various fatty acids to wild-type and JA-deficient mutants confirmed AA as the signaling molecule. Moreover, AA elicited heightened expression of general stress-responsive genes. Importantly, tomato *Solanumlycopersicum* leaves treated with AA exhibited reduced susceptibility to *Botrytiscinerea* infection, confirming AA signaling in other plants. These studies support the role of AA, an ancient metazoan signaling molecule, in eliciting plant stress and defense signaling networks.

S.A. El-Feky

Efficient and selective syntheses of S- Acyl Glutathiones

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ABSTRACT
Selective syntheses of S-acyl glutathiones are achieved in 79-98% yields using 1-acyl-1 H benzotriazoles in the presence of potassium bicarbonate in aqueous methanol at 20 °C. N-Acylation of S-(p-nitrobenzoyl) glutathione with 1 -acyl-1 /H benzotriazoles followed by deprotection of the p nitrobenzoyl groups under mild conditions gave 63-78% yields of W-acyl glutathiones. These methodologies should be useful for the S-acylation and N-acylation of peptides and glycopeptides.

Key words: amino acids, acylation, glutathione, peptides, drugs

Hoda E. Mohamed

Obesity and neurodegeneration: effect of a Mediterranean dietary pattern

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Obesity is a serious global health problem and is associated with a variety of chronic diseases. Increasing evidence suggests that obesity increases the risk of Alzheimer's disease. Several studies have shown that a Mediterranean diet is effective in reducing weight and epidemiological data suggest that such a diet is associated with lower risk of neurodegenerative disorders, including Alzheimer's disease. Therefore, we examined the relationship between obesity and neurodegeneration and the possible
effects of Mediterranean diet on both in adult obese rats. Obese rats showed significant dyslipidaemia, insulin resistance, down-regulation of adiponectin mRNA expression in adipose tissue, up-regulation of brain amyloid precursor protein, apolipoprotein E and caspase-3 mRNA expression and a marked increase in brain oxidative stress. Treatment with Mediterranean diet induced significant weight loss and improvement in these various markers. The present study suggests that Mediterranean diet is a viable nutritional intervention in obesity and, more importantly, in the prevention and treatment of Alzheimer's disease.

**Keywords:** obesity, neurodegeneration, Mediterranean diet, APR, apoE, caspase-3

**Sahar E. El-Swefy**

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Rank: C

**Biochemical effect of a ketogenic diet on the brains of obese adult rats**

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**ABSTRACT**

Excess weight, particularly abdominal obesity, can cause or exacerbate cardiovascular and metabolic disease. Obesity is also a proven risk factor for Alzheimer's disease (AD). Various studies have demonstrated the beneficial effects of a ketogenic diet (KD) in weight reduction and in modifying the disease activity of neurodegenerative disorders, including AD. Therefore, in this study we examined the metabolic and neurodegenerative changes associated with obesity and the possible neuroprotective effects of a KD in obese adult rats. Compared with obese rats fed a control diet, obese rats fed a KD showed significant weight loss, improvement in lipid profiles and insulin resistance, and upregulation of adiponectin mRNA expression in adipose tissue. In addition, the KD triggered significant downregulation of brain amyloid protein precursor, apolipoprotein E and caspase-3 mRNA expression, and improvement of brain oxidative stress responses. These findings suggest that a KD has anti-obesity and neuroprotective effects.

Keywords: Alzheimer disease Amyloid protein precursor Apolipoprotein E Ketogenic diet Neurodegeneration Obesity

**D. HAMDAN**

*Phannazie (2010), 65 (1-7)*  
Rank: C

**Chemical composition of the essential oils of two Citrus species and their biological activities**

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Essential oils obtained by hydrodistillation of the fruit rinds of *Citrus jambhiri* Lush. (Rough lemon) and *C. pyriformis* Hassk (Ponderosa lemon) were analyzed by capillary gas chromatography (GLC/FID) and gas chromatography-mass spectrometry (GLC/MS). A total of 94 compounds were unambiguously identified from the oils and the (hexane/ether) extracts of the rind and juices representing 98.55% and 97.98% of the total oil composition. The main component of both oils was o-limonene (92.48% and 75.56% respectively). The antioxidant, anti-inflammatory, antitrypanosomal, antimicrobial and cytotoxic activities of the essential oils were evaluated. Whereas *Citrus jambhiri* and *C. pyriformis* have antioxidant activity with IC$_{50}$ ±SD 37.69 ±0.21 mg/ml and 28.91 ±0.09 mg/ml, respectively, ascorbic acid a known potential inhibitor for DPPH free radical and commonly used antioxidant has a value of 16.32 ±0.16 µg/ml. Both oils inhibited the activity of 5-lipoxygenase (5-LOX) with an IC$_{50}$ of 40 ± 1.63 and 38 ± 0.82 µg/ml, respectively, and could be considered as interesting candidates for antiinflammatory agents. The essential oils of both species showed substantial antimicrobial activity against all tested Gram positive bacteria and yeasts. The essential oil of *C. pyriformis* shows higher cytotoxic activity against tested cell lines than that of *C. jambhiri*. The IC$_{50}$ values were 374.36 ±43.95 µg/ml and 588.06 ±27.12 µg/ml in case of HepG2 cells and 213.87 ±18.50 µg/ml and 512.45 ± 61.46 µg/ml in case of MIA-PaCa-2 cells respectively.

Nader E. Abo-Dya

Organic and biomolecular. Chem.

The chemical ligation of selectively S-acylated cysteine peptides to form native peptides via 5-, 11- and 14-membered cyclic transition stalest

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Cysteine and C-terminal cysteine peptides are selectively S-acylated at 0-20 °C by A’-(Pg-a-aminoacyl)beizotriazoles to give N-Pg-S-acyl-isodi-, -isotri-, and -isotetra-peptides isolated in good yields. A’-Fmoc-5-acyl-isopeptides are Fmocdeprotected to afford free S-acyl-isopeptides isolated in high yields. 5-Acyl-isodi-, S-acyl-isotetra-, and 5-acyl-isopenta-peptides undergo chemical ligation; migration of the cysteine S-acyl groups to the N-terminal amino acids via 5-, 11-, and 14-membered transition states giving the corresponding native di-, tetra-, and penta-peptides. By contrast, the S-acyl-isotrippeptide prefers intermodular acylation from one molecule to another over an 8-membered intramolecular transition state. The developed methodology allows convenient isolation of stable, unprotected 5-acyl cysteine peptides including the first isolation of S-acyl-isopeptides, which should facilitate the investigation of ligation by physical organic chemistry techniques.