Title: Proniosomes as a Drug Carrier for Transdermal Delivery of Ketorolac

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Source: *European Journal of Pharmaceutics and Biopharmaceutics, 59, 485-490 (2005)*

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Niosomes are nonionic surfactant vesicles that have potential application in the delivery of hydrophobic and hydrophilic drugs. Permeation of a potent nonsteroidal anti-inflammatory, ketorolac, across excised rabbit skin from various proniosome gel formulations was investigated using Franz diffusion cells. Each of the prepared proniosomes significantly improved drug permeation and reduced the lag time ($p<0.05$). Proniosomes prepared with Span 60 provided a higher ketorolac flux across the skin than did those prepared with Tween 20 (7-and 4-fold the control, respectively). A change in the cholesterol content did not affect the efficiency of the proniosomes, and the reduction in the lecithin content did not significantly decrease the flux ($p>0.05$). The encapsulation efficiency and size of niosomal vesicles formed by proniosome hydration were also characterized by specific high performance liquid chromatography method and scanning electron microscopy. Each of the prepared niosomes achieved about 99% drug encapsulation. Vesicle size was markedly dependent on the composition of the proniosomal formulations. Proniosomes may be a promising carrier for ketorolac and other drugs, especially due to their simple production and facile up.

Title: Improvement of Absorption Enhancing Effects of *n*-dodecyl-β-D-maltopyranoside by its Colon-Specific Delivery Using Chitosan Capsules

Authors: Gihan Fetih[1,2], Sara Lindberg[3], Katsuhito Itoh[4], Naoki Okada[1], Takuya Fujita[1], Fawsia Habib[2], Per Artursson[3], Mohammed Attia[2], Akira Yamamoto[1]

Source: *International Journal of Pharmaceutics, 293, 127-135 (2005)*

Address: [1]Department of Biopharmaceutics, Kyoto Pharmaceutical University, Kyoto, Japan, [2]Department of Pharmaceutics, Faculty of Pharmacy, Assiut University, Assiut, Egypt and [3]Department of Pharmacy, Uppsala University, Uppsala, Sweden, [4]Aicello Chemical Co., Ltd., Toyohashi, Aichi, Japan

In general, absorption enhancing effects of various absorption enhancers were greater in the large intestine than those in the small intestinal regions. Therefore, the effectiveness of absorption enhancers is expected to be remarkably observed, if these enhancers can be delivered to the large intestine with some poorly absorbable drugs after oral administration. In this study, therefore, we examined whether chitosan capsules were effective for the colon-specific delivery of a certain absorption enhancer and can improve the absorption enhancing action of the absorption enhancer after oral administration. 5(6)-Carboxyfluorescein (CF) was used as a model drug to investigate the site-dependent effectiveness of various absorption enhancers by an in situ closed loop method. Sodium glycocholate (NaGC), n-dodecyl-β-D-maltopyranoside (LM), sodium salicylate

(NaSal) and sodium caprate (NaCap) were used as models of absorption enhancers in this study. Overall, the absorption enhancing effects of these enhancers for intestinal absorption of CF were greater in the colon than those in the jejunum and the ileum. Especially, among these enhancers tested in this study, LM showed much greater absorption enhancing effect in the colon than in the jejunum and the ileum. Therefore, LM was selected as a model absorption enhancer to examine the effect of chitosan capsules on the absorption enhancing effect of LM. When CF and LM were orally administered to rats using chitosan capsules, the plasma concentration of CF was much higher than those in other dosage forms including solution and gelatin capsules. Therefore, chitosan capsules may be useful carriers for colon-specific delivery of LM, thereby increasing its absorption enhancing effect from the intestinal membranes.

Title: Nitric oxide Donors can Enhance the Intestinal Transport and Absorption of Insulin and [Asu[1,7]]-eel Calcitonin in Rats

Authors: Gihan Fetih[1,2], Fawsia Habib[2], Naoki Okada[1], Takuya Fujita[1], Mohammed Attia[2], Akira Yamamoto[1]

Source: *Journal of Controlled Release, 106, 287-297 (2005)*

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The characteristics of three NO donors, 3-(2-hydroxy-1-(1-methylethyl)-2-nitrosohydrazino)-1-propanamine (NOC5), N-ethyl-2-(1-ethyl-2-hydroxy-2-nitrosohydrazino)-ethanamine (NOC12) and S-nitroso-N-acetyl-DL-penicillamine (SNAP) as absorption enhancers for peptide drugs were examined in rats using a modified Ussing chamber method and an in situ closed loop method. Insulin and [Asu[1,7]]-eel calcitonin (ECT) were used as a model drug to investigate the effectiveness of the tested enhancers. The NO donors significantly increased the in vitro permeability of insulin across all intestinal membranes. In general, the absorption enhancement effects of these NO donors were greater in the colon than those in the jejunum and ileum. Of these NO donors, SNAP was the most effective enhancer. Their effects were concentration-dependent over the range of 0.01 to 0.1 mM. However, 0.1 mM NO donors had almost the same effects as those at 1 mM concentration. The absorption enhancing effects of the three NO donors were inhibited by the co-administration of 2-(4-carboxyphenyl)-4,4,5,5-

tetramethylimidazole-1-oxyl 3-oxide, sodium salt (carboxy-PTIO), an NO scavenger, suggesting that NO might be responsible for the efficacy of NO donors. In the in situ closed loop experiments, the three enhancers significantly improved the pharmacological availability % (PA%) of insulin in the small and large intestine. Similar results were also obtained when NO donors were added to ECT solution by an in situ closed loop method. These results suggest that NO donors possess excellent effectiveness for the use as absorption enhancers of peptide drugs and they are very effective at lower concentrations compared to the conventional enhancers.

Title: Evaluation of a Novel Vaginal Bromocriptine Mesylate Formulation: A Pilot Study

Authors: Atef M. Darwish[1], Ehsan Hafez[2], Ibraheem El-Gebali[2], Sahar B. Hassan[2]

Source: *Fertility and Sterility, 83 (4), 1053-1055 (2005)*

Address: [1]Department of Obstetrics and Gynaecology, Faculty of Medicine, and [2]Department of Pharmaceutics, Faculty of Pharmacy, Infertility Outpatient Clinic, Mother-Health Hospital, Assiut University, Assiut, Egypt

Because of the frequent side effects found with oral bromocriptine, we created two formulas of vaginal bromocriptine suppositories to compare with vaginal application of bromocriptine tablets. The formula containing bromocriptine and a releasing agent (Pluronic F127) showed an increased dissolution rate, 39-fold greater than that of the pure drug alone, and subsequently was effective in lowering serum prolactin.

Title: Formulation and Evaluation of Famotidine Sublingual Tablets

Authors: M. A. Hassan, A. S. A. Ibrahim, M. G. Abd El-Mohsen, S. M. El-Shanawany

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 149-157 (2005)*

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

Formulation of famotidine, rapidly disintegrated sublingual tablets, by direct compression was carried out. Fifteen tablets formulae were made in order to obtain suitable non-friable formulae, with disintegration time less than one minute and average crushing strength of 2-4 kg/cm^2. The excipients used in the different formulae are Avicel pH101, sorbitol, mannitol, lactose anhydrous, Ac-Di-Sol, magnesium strearate and saccharin sodium. The formulae prepared were tested for the effect of certain excipients on the hardness, friability and disintegration time. Tablets of 20 mg famotidine from the formulated and commercial oral dosage forms were administered to five healthy volunteers participated in the study using a balanced cross-over design. Comparison of the mean urinary excretion rate obtained after administration of both dosage forms indicated that in both cases, the time taken to reach peak occurred at a mid point of 1.5 hours. Comparison of the cumulative amounts excreted in the urine after administration of famotidine in the two different dosage forms revealed that about 5.49±1.06 mg of the administered dose (20 mg) was recovered unchanged in the urine during 12 hours following sublingual tablets administration. This value was found to be higher than that excreted after administration of Pepcid® oral

tablets (4.61±0.65 mg) during the same period of time. Statistical analysis of the difference at P= 0.05, revealed non-significant difference in the urinary excretion rate obtained of the two different dosage forms. On the other hand, a significant difference was found to exist in the total cumulative amount of famotidine excreted in the urine at 2 and 6 hours from both dosage forms. The results also indicated that there was no significant difference in AUC_{0-12} between the two dosage forms.

Title: Formulation and Evaluation of Croconazol Hydrochloride Topical Gels

Authors: M. EL-Badry[1], and N. A. Hussein[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 283-289 (2005)*

Address: [1]Department of Pharmaceutics, Faculty of Pharmacy and [2]Department of Botany, Faculty of Science, Assiut University, 71526 Assiut, Egypt

This study was designed to evaluate different polymers for their suitability as a vehicles for topical drug delivery systems. Croconazol hydrochloride is an azol derivative used as antimycotic agent. It was incorporated in this vehicles as a gel forms in a concentration of 1.0% w/w. Polymers used in this study are methylcellulose (MC), Tylose (Ty), Polyvinyl alcohol (PVA), Pluronic F-127 (pl. F-127), Polyethylene glycol (PEG), Carbopol 974P (Carb.) and Eudispert mv. (Eud). They were used in a suitable concentration for gel formulation.

In-vitro release characteristics of the drug from different gels were carried out using dialysis membrane in phosphate buffer pH 5.2. The release data were treated with various kinetic principles to assess the relevant parameters. The general rank order of Croconazol hydrochloride release from the prepared gel were MC > Ty > pl. F-127 > PVA > Carb > Eud > PEG. The results showed that, the release of drug from the prepared gels obeyed the diffusion model (Higuchi's equation). Some kinetic parameters were calculated such as diffusion coefficient, permeability coefficient and the partition coefficient. The results indicated a direct dependence of the release rate on the diffusion coefficient. The influence of initial drug concentration (0.5, 1.0 and 2.0% w/w), and pl F-127 concentration

(20, 25, 30% w/v) on the release patterns was studied. The obtained data revealed an inverse correlation between the drug release rate and the pluronic F-127 concentration and a direct correlation between the drug release rate and the initial drug concentration. The anti-fungal activity of the different gel formulations was evaluated by agar-cup plate technique using five fungal species. The results obtained indicated that, all gel formulations have good anti-fungal activities.

Title: Caffeic Acid Phenethyl Ester Modulates Helicobacter Pylori-induced Nuclear Factor-kappa B and Activator Protein-1 Expression in Gastric Epithelial Cells

Authors: Mohamed M. Abdel-Latif[1], Henry J. Windle[1], Basma S. El Homasany[1], Kamal Sabra[2], Dermot Kelleher[1]

Source: *British Journal of Pharmacology, 146, 1139-1147 (2005)*

Address: [1]Department of Clinical Medicine, Dublin Molecular Medicine Centre and Trinity Centre for Health Sciences, St James's Hospital, Dublin 8, Ireland and [2]Department of Pharmacy, St James's Hospital, Dublin 8, Ireland

Caffeic acid phenethyl ester (CAPE), an active component of propolis from honeybee hives (honeybee resin), has anti-inflammatory, anti-carcinogenic and anti-bacterial properties. This study was designed to investigate the anti-inflammatory effects of CAPE on Helicobacter pylori-induced NF-κB and AP-1 in the gastric epithelial cell line AGS.

Electrophoretic mobility shift assay was used to measure NF-κB and AP-1 DNA- binding activity. Western blotting was used to detect IκB-α and COX-2 expression in AGS cells cocultured with H. pylori. The antiproliferative effect of CAPE was measured by MTT assay.

Our results showed that caffeic phenethyl ester inhibits H. pylori-induced NF-κB and AP-1 DNA-binding activity in a dose (0.1-25 μg ml^{-1} ~0.35-88 μM) and time- (15-240 min) dependent manner in AGS cells. Maximum inhibition by

CAPE was observed at concentrations of 25 μg ml^{-1} (~88 μM) CAPE prevented H. pylori- and cytokine-induced degradation of $I_{\kappa}B$-χ protein

Pretreatment of AGS cells with CAPE also blocked cytokine- and mitogen-induced NF-$_{\kappa}$B and AP-1 expression. Furthermore, CAPE suppressed H. Pylori-induced cell proliferation and production of the cytokines TNF-α and IL-8. In addition, CAPE blocked H.Pylori-induced COX-2 expression.

The inhibition of such transcription by CAPE could result in suppression of many genes during H. pylori-induced inflammation, and also provide new insights into the anti-cancer and anti-inflammatory properties of CAPE.

Title: Proinflammatory Cytokine and Nuclear Factor Kappa-B Expression Along the Inflammation-Metaplasia-Dysplasia-Adenocarcinoma Sequence in the Esophagus

Authors: J. M. O'Riordan, M. M. Abdel-Latif, N. Ravi, D. McNamara, P. J. Byrne, G. S. A. McDonald, P. W. N. Keeling, D. Kelleher, J. V. Reynolds

Source: *Am. J. Gastroenterol., 100, 1257-1264 (2005)*

Address: University Departments of Surgery, Pathology and Medicine, St James's Hospital, the Dublin Molecular Medicine Centre, Trinity College, Dublin, Ireland

Background: *The incidence of esophageal adenocarcinoma has increased significantly in the western world over the last 20 yr. Most cases arise in a background of chronic gastroesophageal reflux, and specialized intestinal metaplasia in Barrett's esophagus is frequently an antecedent phenotype or evident in association with adenocarcinoma. The molecular events that characterize the pathway from inflammation to metaplasia to dysplasia and adenocarcinoma are poorly understood.*

Aims: *To examine the expression of the proinflammatory cytokines IL-8 and IL-1β along the esophagitis, metaplasia, dysplasia, and adencarcinoma pathway, and to correlate this with histological changes and expression of the transcription factor NF-κB.*

Patients and Methods: *Fresh biopsy specimens were collected from patients with reflux esophagitis (n=15), Barrett's esophagus (n=35), Barrett's adjacent to adenocarcinoma (n=8), and esophageal adenocarcinoma (n-35). IL-8 and IL-1β*

expression were measured using enzyme-linked immunosorbent assay. NF-κB expression was measured by electrophoretic mobility shift assay.

***Results**: Elevated expression of NF-κB was found in 2 (13%) out of 15 patients with reflux esophagitis, 21 (60%) out of 35 patients with Barrett's esophagus, and 28 (80%) out of 35 patients with esophageal adenocarcinoma. All 5 patients with Barrett's esophagus and high-grade dysplasia showed elevated expression of NF-κB. IL-8 and IL-1β were significantly increased in esophagitis, Barrett's and adencarcinoma compared with squamous epithelium, and in adencarcinoma compared with all other groups. There was a stepwise increase in the expression of IL-8, IL-1β, and NF-κB from normal through Barrett's epithelium to adenocarcimoma in eight cases of esophageal adenocarcimoma. The levels of both IL-8 and IL-1β in adenocarcinoma patients correlated with stage of disease. Patients with adenocarcinoma who were NF-κB positive had significantly higher levels of both IL-8 (p= 0.04) and IL-1β (p= 0.03) compared to adenocarcimoma patients who were NF-κB negative.*

***Conclusions**: The proinflammatory cytkines IL-8 and IL-1β are elevated in esophagitis and Barrett's epithelium, and markedly elevated in adenocarcinoma. NF-κB activation is infrequent in esophagitis, but is increased in Barrett's epithelium and adenocarcinoma. The association of NF-κB activation with cytokine upregulation was only evident in patients with adenocarcinoma. These patterns may play an important role in Barrett's inflammation and tumourigenesis, and inhibition of the NF-κB/proinflammatory cytokine pathway may be an important target for future chemoprevention strategies.*

Title: Activated Nuclear Factor-kappa B and Cytokine Profiles in the Esophagus Parallel Tumor Regression Following Neoadjuvant Chemoradiotherapy

Authors: M. M. M. Abdel-Latif[1], J. M. O'Riordan[1], N. Ravi[1], D. Kelleher[2], J. V. Reynolds[1]

Source: *Diseases of Esophagus, 18, 246-252 (2005)*

Address: [1]Departments of Clinical Surgery and Clinical Medicine and [2]Dublin Molecular Medicine Centre, Trinity Centre for Health Science, St James's Hospital and Trinity College Dublin, Ireland

Esophageal adenocarcinoma is increasing in incidence; it relates to chronic gastroesophageal reflux, it is difficult to cure, and treatment modalities increasingly use chemotherapy and radiation therapy prior to resectional surgery. Nuclear factor-Kappa B (NF-κB) is a pleiotropic transcription factor that regulates several genes for cytkines and enzymes involved in inflammation and immunity, and we have previously described sequential expression of NF-κB from the normal esophagus through Barrett's metaplasia to adenocarcinoma. The aim of this exploratory study was to assess the NF-κB status and cytokine profiles pre- and post-chemoradiotherapy for esophageal adenocarcinoma. Fresh biopsy specimens obtained from 20 patients with esophageal adenocarcinoma and normal adjacent squamous epithelium were obtained pre, during and post-chemoradiotherapy, and NF-κB expression was analyzed by electrophoretic mobility shift assay. The cytokine protein content of interleukin-1 beta (IL-1β) and interleukin-8 (IL-8) of tissue homogenates was measured using the ELISA

technique, NF-κB was constitutively activated in tumor tissues from esophageal adenocarcinoma but was not detected in adjacent normal esophageal mucosa. Elevated levels of IL-1β and IL-8 were significantly ($p < 0.05$) higher in tumor tissues compared to control tissues. Patients with a major or complete pathological response (responders) were associated with absence of activated NF-κB from nuclear extracts after treatment. Moreover, IL-1β and IL-8 levels were significantly ($p < 0.05$) down-regulated in tumor tissues from patients who demonstrated a complete pathological response. No differences in NF-κB, IL-1β and IL-8 levels were detected pre- and post- treatment in patients who did not have a major or complete pathological response (non-responders). The study suggests that monitoring of molecular and cytokine patterns in patients undergoing this neoadjuvant regimen may help subselect the cohort that derives most benefit from the multimodal approach.

Title: Low pH and Helicobacter Pylori Increase Nuclear Factor Kappa B Binding in Gastric Epithelial Cells: A Common Pathway for Epithelial Cell Injury

Authors: Dermot O'Toole[1], Mohammed M. M. Abdel-Latif[1], Aideen Long[2], Henry J. Windle[1], Anne M. Murphy[1], Andrew Bowie[3], Luke A. J. O'Neill[3], Donald G. Weir[1], Dermot Kelleher[1]

Source: *Journal of Cellular Biochemistry, 96, 589-598 (2005)*

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Helicobacter Pylori infection results in peptic ulceration and chronic gastritis through mechanisms which are not fully elucidated. Live H. pylori activate the pro-inflammatory transcription factor NF-κB in gastric epithelial cells. Patients may have peptic ulcer disease in the absence of H. pylori infection; therefore other factors contribute to the inflammatory process. Maximal acid output in patients with H. pylori infection and duodenal ulceration is significantly increased indicating a role for acid in the pathogenesis of mucosal ulceration. The effect of low pH on NF-κB activation in gastric epithelial cells has not been studied. Human gastric epithelial cells (AGS) were exposed to a range of pH changes in the presence or absence of H. pylri. NF-κB DNA binding and cytosolic IκB-α were measured using electrophoretic mobility shift assay and Western blotting.

NF-κB DNA-binding in gastric epithelial cells dramatically increased when the pH of the culture medium decreased. Increases in NF-κB nuclear binding were paralleled by decreasing amounts of cytosolic IκB-α. Theses findings were similar but less potent than those observed when cells were exposed to H.pylori. low pH resulted in enhancement of H. pylori-induced NF-κB nuclear binding. DNA binding of NF-κB activation secondary to low pH was attenuated by PD98059 but nor by SB203580. Similar to H. pylori, low pH potently and independently augments NF-κB nuclear binding in AGS cells and such activation appears to be mediated through MEK1-dependant signaling pathways.

Title: Vitamin C Enhances Chemosensitization of Esophageal Cancer Cells *in Vitro*

Authors: M. M. M. Abdel-Latif[1], A. A. Raouf[1], K. Sabra[2], D. Kelleher[3] and J. V. Reynolds[1]

Source: *Journal of Chemotherapy, 17 (5), 539-549 (2005)*

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Chemotherapy is increasingly utilized in multimodal protocols to try and improve outcomes. Cisplatin and 5-fluorouracil (5-Fu) are the mainstay of chemotherapeutic regimens, and an understanding of sensitivity and resistance of esophageal cancer to these agents is of considerable clinical importance. Antioxidants may modulate the response to chemotherapy, and in this study we examined the effect of vitamin C on 5-Fu and cisplatin cytotoxicity and related pathwaysin the esophageal cancer cell lines OE33 and SKGT-4. The antiproliferative effect of antitumor agents was measured by the MTT assay, and the transcription factors NF-κB and AP-1 pathways were assessed by electrophoretic mobility gel shift assay. 5-Fu and cisplatin demonstrated marked morphological changes and decreased cell proliferation. A combination of vitamin C with 5-Fu or cisplatin exerted a significantly enhanced cytotoxic effect compared to both drugs individually. Treatment of esophageal cancer cells with 5-Fu and cisplatin induced NF-κB and AP=1 activation. Pretreatment with vitamin C inhibited 5-Fu or cisplatin induced NF-κB nuclear translocation and DNA binding activity, but vitamin C had no effect on IκB-α protein levels.

Vitamin C also inhibited 5-Fu- and cisplatin-induced AP-1 activation. Our data demonstrate that vitamin C enhances the antitumor activity of 5-Fu and cisplatin, in part by inhibiting translocation of NF-κB and AP-1, and sensitizes cancer cells to drug-induced cell death. The data suggest that vitamin C supplementation may improve the efficacy of chemotherapy for esophageal cancer.

Title: Chemical Constituents of *Gladiolus segetum* Ker-Gawl

Authors: Khaled M. Mohamed

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 71-78 (2005)*

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

*From the chloroform soluble fraction of the methanolic extract of the corms of Gladiolus segetum Ker-Gawl (Iridaceae), nine compounds were isolated and identified as follows: the lignans (+)-demethoxypinoresinol (**1**), (+)-pinoresinol (**2**) and (+)-pinoresinol monomethylether (**3**); the neolignan (–)-dehydrodiconiferyl alcohol (**4**) and the anthraquinones deoxy-erythrolaccin (**5**), physcion (**6**) and laccaic acid D methylester (**7**) together with 6'-O-palmitoyl-3-O-β-sitosterol glucoside (**8**) and β-sitosterol-3-O-glucoside (**9**). The structures of the isolated compounds were determined by physical and spectroscopic methods including NMR and MS spectral analysis. Compounds **1-4** and **6-9** are reported here for the first time from the genus Gladiolus while compound **5** was previously isolated from the same plant.*

Title: Xanthones From Cell Cultures of *Hypericum gnidioides* Seem.

Authors: A. M. A. Abd El-Mawla

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 105-111 (2005)*

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

Oxygenated and prenylated xanthones were isolated from the cell cultures of Hypericum gnidioides Seem. when grown in modified B5 medium in the dark. Based on the spectral methods, the structure of the isolated compounds were elucidated as 1,7-dihydroxyxanthone (euxanthone), 1,3,7-trihydroxyxanthone, 1,3,5,6-tetrahydroxyxanthone, 1,3,6,7-tetrahydroxy-8-(3-methylbut-2-enyl) xanthone and 1,3,6,7-tetrahydroxy-2,8-di(3-methylbut-2-enyl) xanthone (γ-mangostin). The occurrence of both 1,7-dihydroxyxanthone and 1,3,7-trihydroxyxanthone which is recorded for the first time in cell cultures of Hypericum species indicate the presence of a reductase activity responsible for eliminating the 3-hydroxy group and confirm the biosynthetic pathway of xanthones in Hypericum species respectively.

Title: Biotransformation of Flavonols to Flavonols-3-O-Glucoside in Cell Cultures of *Astragalus sieberi* DC.

Authors: A. M. A. Abd El-Mawla, Zedan Z. Ibraheim

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 113-117 (2005)*

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One distinct glucosyltransferase (GT) has been partially purified and characterized from cell cultures of Astragalus sieberi DC.; Family Leguminosae. Callus cultures were established from shoots of sterile germinated seeds maintained on solid MS medium supplemented with 4.5 μM 1-naphthylacetic acid (NAA) and 2.3 μM kinetin (KIN). The cell suspension cultures were obtained by transport of callus cultures to liquid MS medium with the same hormone supplementation. The GT was found to exhibit maximum activity at pH 7.5 and an incubation temperature of 35°C. The preferred substrate of GT was found to be kaempferol, the second best substrate was quercetin. The isolated enzymatic products were detected by TLC and HPLC and identified by spectral analysis and comparison with authentic compounds.

This experiment from economic point of view provides the best conditions for large scale production of glucosides of kaempferol, quercetin and isorahmnetin.

Title: Phenylethanoid Glycosides from *Barleria cristata* L. Callus Cultures

Authors: A. M. A. Abd El-Mawla[1], A. S. Ahmed[1], Z. Z. Ibraheim[1], L. Ernst[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 199-204 (2005)*

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Three phenylethanoid glycosides viz; β-[(3',4'-dihydroxyphenyl)-ethyl]-(4''-O-caffeoyl)-β-D-glucoside (desrhamnosylacteoside) ***(1)****, β-[(3',4'-dihydroxyphenyl)-ethyl]-(3''-O-L-rhamnosyl)-(4''-O-caffeoyl)-β-D-glucoside (acteoside)* ***(2)*** *and β-[(3',4'-dihydroxyphenyl)-ethyl]-(3'',6''-O-L-dirhamnosyl)-(4''-O-caffeoyl)-β-D-glucoside (poliumoside)* ***(3)*** *were isolated and identified from the callus cultures of Barleria cristata L.The structures of the isolated compounds were established by spectroscopic evidence (UV, 1D and 2D-NMR and ESIMS), further confirmation has been done by comparison with authentic samples. The amount of compounds 1-3 were determined in the callus culture using HPLC.*

Title: Macro- and Micromorphology of Leaf, Stem and Root of *Polygonum bellardii* ALL Growing in Egypt

Authors: M. H. Mohamed[1], Z. Z. Ibraheim[2], A. M. A. Abd El-Mawla[2], A. M. Abd El-Kader[1]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 297-310 (2005)*

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The macro- and microrphological characters of the leaf, stem, and root of Polygonum bellardii All. growing in Egypt are presented with the aim of finding out the charactrers by which the plant could be identified in both the entire and powdered forms.

Title: Synthesis, Analgesic and Anti-Inflammatory Activities of 4-Oxo-4-(4-(Pyrimidin-2-Yl)Piperazin-1-Yl)Butanic Acid Derivatives

Authors: Hamdy M. Abdel-Rahman, Mahmoud M. Sheha

Source: *Medicinal Chemistry: An Indian Journal, 1 (1-2), 7-13 (2005)*

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A series of 4-Oxo-4-(4-(pyrimidin-2-Yl)piperazin-1-Yl)butanic acid derivatives were synthesized and tested for their analgesic and anti-inflammatory activities, cyclooxygenase inhibition as well as for their ulcerogenic potential.

Title: Allophenylnorstatine-Containing HIV-1 Protease Inhibitors: Design, Synthesis and Structure-Activity Relationships for Selected P_2 Ligands

Authors: Hamdy M. Abdel-Rahman[1], Nawal A. El-Koussi[1], Gamal S. Alkaramany[1], Adel F. Youssef[1], Yoshiaki Kiso[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 95-103 (2005)*

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The design and development of potent HIV protease inhibitors remain an attractive target for antiviral therapy. A novel class of HIV protease inhibitors containing allophenylnorstatine [Apns; (2S,3S)-3-amino-2-hydroxy-4-phenylbutyric acid] as a transition state mimic have been reported. In this work we fixed P_2` (as tert-butylamino or 2-methylbenzylamino) and changed P_2 moiety to provide two series of dipeptide analogs. Preliminary evaluation of the activity of the synthesized derivatives were determined as percentage of enzyme inhibition at 5 μM level. The results showed that the introduction of 2-methylbenzylamino moiety as P_2` ligand ***6a-e*** *considerably improved HIV inhibitory activity in comparison with the tert-butyl amino analogs* ***5a-e****. It was found that compounds in both series retained activity still less than the lead compounds KNI-577 and KNI-727.*

Title: Synthesis and Anti-Inflammatory Testing of Some New Compounds Incorporating 5-Aminosalicylic Acid (5-ASA) as Potential Prodrugs

Authors: Abdel-Alim Mohamed Abdel-Alim, Abdel-Nasser Ahmed El-Shorbagi, Samia Galal Abdel-Moty, Hajjaj Hassan Mohamed Abdel-Allah

Source: *Arch Pharm. Res., 28 (6), 637-647 (2005)*

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*This work includes the synthesis of 15 final compounds (**6a-h** and **7b-h**) as prodrugs of 5-ASA in the form of the acid itself, esters and amides linked by an amide linkage through a spacer to the endocyclic ring N of nicotinamide. Also, 15 new intermediate compounds were prepared. The target compounds (**6b, 6f, 7b** and **7e-h**) revealed potent analgesic and anti-inflammatory activities in comparison to sulfasalazine and 5-ASA. In addition, ulcerogenicity, LD_{50}, in vivo and in vitro metabolism of compound **7f** were determined.*

Title: Synthesis and Antimicrobial Activity of Some 3,5-Disubstituted-Tetrahydro-2H-1,3,5-Thiadiazine-2-Thione Derivatives

Authors: Samia G. Abdel-Moty

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 9-15 (2005)*

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Twelve new 3-(isobutyl)-5-substituted-tetrahydro-2H-1,3,5-thiadiazine-2-thiones were synthesized by the reaction of isobutylamine with carbon disulfide and potassium hydroxide, followed by formaldehyde and appropriate alkyl, cycloalkyl aralkyl amines, amino acid, and INH. Their structures have been elucidated by spectral data and elemental analysis. The title compounds were tested for antimicrobial activity in vitro against gram-positive bacteria (Staphylococcus aureus,and Micrococcus leuteus), gram-negative bacteria (Serratia marcescens and Escherichia coli) and some fungi (Candida albicans, Scopulariopsis brevicalus, Geotrichum candidum, Macrophomina phaseolina, Fusarium oxysporum and Trichoderma harzianum) using agar cup diffusion method. The antimicrobial activity was found to be greatly affected by the bulkiness of the side chain and the presence of polar carboxylic group. Highest activity was obtained with compounds **4a** *and* **4k** *(R= CH_3, CH_2-COOH).*

Title: Synthesis of Some New 1,4-Disubstituted Piperazine-2,3-Dione Derivatives of Potential Anthelmintic Activity

Authors: Mostafa A. Hussein[1], Ahmed K. Diab[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 37-44 (2005)*

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*The purpose of this study based upon design and synthesis of a new series of 1,4-disubstituted piperazine-2,3-dione derivatives through two steps reaction. This protocol involves the formation of N,N\-Bis-(4-substituted benzyl)-ethane-1,2-diamine and N,N\-Bis-[1-(4-substituted phenyl)-ethyl]-ethane-1,2-diamine derivatives (**1a-i**) through reductive alkylation reaction from ethylenediamine and different carbonyl compounds in the presence of sodium cyanoborohydride. The second step involves reaction of compounds (**1a-i**) with diethyl oxalate affording the target compounds. Consequently, nine new 1,4-disubstituted piperazine-2,3-dione derivatives were synthesized as the target compounds, 1,4-Bis-(4-substituted benzyl)-piperazine-2,3-dione and 1,4-Bis-[1-(4-substituted phenyl)-ethyl]-piperazine-2,3-dione derivatives (**2a-i**). The structures of the target compounds were elucidated depending upon the data of the different spectral as well as the elemental methods of analyses. In addition, a mass spectrum, for a representative example, was carried out where the expected fragmentation pattern is in accordance with the structure of the considered compound. The lipophilicity of the target compounds as expressed from the ClogP and the measured R_f*

*remarkably supercede that of piperazine. The preliminary anthelmintic activity of the newly synthesized derivatives (**2a-i**) was investigated in vitro against Enterobiuos vermicularis and Fasciola hepatica. The tested compounds exhibited, in all cases, considerable inhibitory effects on the growth of the tested parasites in comparison with piperazine hydrate as a reference drug.*

Title: Synthesis of Some Quinoline Thiosemicarbazone Derivatives of Potential Antimicrobial Activity

Authors: Samia G. Abdel-Moty[1], Mostafa H. Abdel-Rahman[2], Hosney A. Elsherief[2], Abdel-Hamid N. Kafafy[1]

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 79-93 (2005)*

Address: [1]Department of Pharmaceutical Organic Chemistry, Faculty of pharmacy, Assiut University, Assiut-71527, Egypt and [2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Al-Azhar University, Assiut, Egypt

*5-Acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemicarbazones (**IIa-m, IIIa-m** respectively) have been prepared via the condensation of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline with the appropriate 4-substituted-3-thiosemicabazides (**Ia-l**). The thiosemicarbazones (**IIa-l, IIIa-f**) were subjected to cyclization into the corresponding thiazolidinones (**IVa-l, Va-f**) by the reaction with ethyl bromoacetate in the presence of anhydrous sodium acetate. The structures of the thiosemicarbazones as well as the corresponding thiazolidinones were assigned based on both elemental and spectroscopic evidences. The prepared compounds were also evaluated for antibacterial and antifungal activities.*

Title: Synthesis and Antitubercular Activity of Some Mannich Bases Derived From Isatin Isonicotinic Acid Hydrazone

Authors: Mostafa A. Hussein[1], Tarek Aboul-Fadl[2], Asmma Hussein[3]

Source: *Bull. Pharm. Sci., Assiut University, 28 (1), 131-136 (2005)*

Address: [1]Department of Pharmaceutical Organic Chemistry, [2]Department of Pharmaceutical Medicinal Chemistry, Faculty of Pharmacy and [3]Department of Animal hygiene and Zoonoses, Faculty of Veterinary Medicine, Assiut University, Assiut-71526, Egypt

*The purpose of this study based on the design and synthesis of a new series of 4-[1-(substitutedaminomethyl)]-2-oxo-2,3-dihydro-1H-3-indolylidene-pyridine-carboxylic acid hydrazones (**2a-g**) in a trial to overcome the resistance developed with the therapeutic uses of isonicotinic acid hydrazide (isoniazid, INH). The new compounds were prepared by reacting isatin isonicotinic acid hydrazone with formalin and the appropriate secondary amines. The structures of the newly synthesized compounds were elucidated using different spectral data (IR, ^{1}HNMR, and ^{13}CNMR) as well as elemental methods of analyses. The lipophilicity of the synthesized compounds supercedes that of INH as expressed by Clog P.*

*The new compounds (**2a-g**) as well as INH as a reference drug were tested for their antitubercular activity against bovine Mycobacterium tuberculosis at a dose level of 10 µmol. The tested compounds exhibited comparable inhibitory activity against the tested TB strain comparing to INH a reference drug.*

Title: Synthesis of Certain 2-Aroylindole Derivatives of Potential Analgesic, Anti-Inflammatory and Antipyretic Activities

Authors: S. G. Abdel-Moty, A. M. Abdel-Aal, A. N. Kafafy, A. A. El-Shorbagi

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 213-223 (2005)*

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In the present study, a series of 2-aroylindole derivatives were synthesized by phase transfer catalysis (PTC) and were characterized by IR, ^{1}H-NMR, Mass spectral and Elemental analysis. Indole derivatives ***6a-g, 7a-f, 8a-f*** *and 9a-13a were tested for analgesic activity using hot-plate test. Compounds 7b and 8b were tested for antipyretic and anti-inflammatory activity using yeast induced hyperthermia and paw edema in rats. Analgesic activity was shown when indole nucleus was substituted at position 2 and 3 by phenyl and (p-halo)benzoyl moieties respectively, where highest activity was recognised in compounds* ***7b*** *and* ***8b****. Both compounds also exhibited faster, more effective and prolonged reduction in hyperthermia and edema induced in rats compared with indomethacin. Compounds* ***7b*** *and* ***8b*** *were also tested for ulcerogenic activity in mice, where a lower ulcerogenic effect was observed compared with indomethacin at all tested dose levels.*

Title: Synthesis of Trigonelline and Nicotinamide Linked Prodrugs of 5-Aminosalicylic Acid (5-ASA) with Analgesic and Anti-Inflammatory Effects

Authors: H. H. M. Abdu-Allah, A. M. Abdel-Alim, S. G. Abdel-Moty, A. A. El-Shorbagi

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 237-253 (2005)*

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

3-N-(4`-Hydroxy-3`-substituted phenyl)carbamoyl-1-methylpyridinium iodides (compds. ***56-j****) and 3-carbamoyl-1-(N-(4`-hydroxy- 3`-substituted phenyl)carbamoyl) methyl pyridinium chlorides (compds.* ***7a-j****) were synthesised and some of them were tested for their analgesic and antiinflammatory activities by hot plate test and carageenin-induced hind paw edema model, respectively. Compound* ***56*** *revealed the most potent analgesic and anti-inflammatory activities in comparison to sulfasalazine (SASP) and 5-ASA. In addition, ulcerogenicity,* LD_{50}*, in-vivo and in vitro cleavage and pH stability of compound* ***56*** *were also determined.*

Title: Synthesis and Antimicrobial Activity of Some 3-(1-Phenylethyl)-5-Substituted-2H-Tetrahydro-1,3,5-Thiadiazine-2-Thione Derivatives

Authors: A. A. Radwan[1], N. A. Hussein[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 255-260 (2005)*

Address: [1]Department of Pharmaceutical Organic Chemistry, Faculty of Pharmacy and [2]Department of Botany, Faculty of Science, Assiut University, Assiut-71527, Egypt

In a search for potential antimicrobial compounds thirteen new 3-(1-phenylethyl)-5-substituted-tetrahydro-2H-1,3,5-thiadiazine-2-thiones were synthesized by the reaction of α-phenethylamine with carbon disulfide and potassium hydroxide, followed by formaldehyde and the appropriate alkyl, aralkylamines, glycine or ethyl glycinate (Scheme 1). The chemical structure of the synthesized compounds was elucidated by spectral data and elemental analysis. The title compounds were tested, in vitro, for antimicrobial activity against Gram-positive, Gram-negative bacteria, and some fungi, using agar disc method. The antimicrobial activity was found to be affected by the bulkiness of the side chain and presence of polar group at N^5 position. The highest activity was obtained with compounds ***4l*** *and* ***4m*** *(R= CH_2-COOH, CH_2-$COOC_2H_5$).*

Title: Development and Validation of Spectrophotometric Methods for Determination of Fluoxetine, Sertraline, and Paroxetine in Pharmaceutical Dosage Forms

Authors: Ibrahim A. Darwish

Source: *Journal of AOAC International, 88 (1), 38 (2005)*

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

Three simple and sensitive spectrophotometric methods were developed and validated for determination of the hydrochloride salts of fluoxetine, sertraline, and paroxetine in their pharmaceutical dosage forms. These methods were based on the reaction of the N-alkylvinylamine formed from the interaction of the free secondary amino group in the investigated drugs and acetaldehyde with each of 3 haloquinones, i.e., chloranil, bromanil, and 2,3-dichloronaphthoquinone, to give colored vinylamino-substituted quinones. The colored products obtained with chloranil, bromanil, and 2,3-dichloronaphthoquinone exhibit absorption maxima at 665, 655, and 580 nm, respectively. The factors affecting the reactions were studied and optimized. Under the optimum reaction conditions, linear relationships with good correlation coefficients (0.9986-0.9999) were found between the absorbances and the concentrations of the investigated drugs in the range of 4-120 μg/mL. The limits of detection for the assays ranged from 1.19 to 2.98 μg/mL. The precision values of the methods were satisfactory; the relative standard deviations were 0.56-1.24%. The proposed methods were successfully applied to the determination of the 3 drugs in pure and pharmaceutical dosage forms with good accuracy; the recoveries ranged from 99.1 to 101.3% with

standard deviations of 1.15-1.92%. The results compared favorably with those of reported methods.

Analytical Chemistry

Title: Spectrofluorimetric Determination of Acetaminophen with N-Bromosuccinimide

Authors: Hanaa M. Abdel-Wadood, Niveen A. Mohamed, Fardous A. Mohamed

Source: *Journal of AOAC International, 88 (6), 1626 (2005)*

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

A simple, sensitive, and selective method for determination of acetaminophen based on its oxidation using N-Bromosuccinimide (NBS) to produce a highly fluorescent product. Optimization of reaction variables was carried out concerning NBS concentration, pH, temperature, reaction time, and stability time. Under optimal analytical conditions, the fluorescent intensity was measured at λemission 442nm (excitation at λ330 nm). The linearity range is 120-800ng/mL with lower detection limit of 33.6 ng/mL acetaminophen. The method was applied successfully to the determination of the compound in pharmaceutical preparation, with average recovery of 100.3 ±2%. The method was also applied successfully to the determination of the drug in spiked plasma samples, with an average recovery of 101.2 ± 1%. Interference effects of some compounds, present in combination with acetaminophen, were studied and the tolerance limits of these compounds were determined.

Title: Analytical Study for the Charge-transfer Complexes of Losartan Potassium

Authors: Ibrahim A. Darwish

Source: *Analytica Chimica Acta, 549, 212-220 (2005)*

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

Studies were carried out, for the first time, to investigate the charge-transfer reactions of losartan potassium (LOS-K) as n-electron donor with the σ-acceptor iodine and various π-acceptors: 7,7,8,8-tetracyanoquinodimethane, 1,3,5-trinitrobenzene, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, p-chloranilic acid, tetracyanoethylene, 2,3,5,6-tetrabromo-1,4-benzoquinone, 2,3,5,6-tetrachloro-1,4-benzoquinone, and 2,4,7-trinitro-9-fluorenone. Different colored charge-transfer complexes and radical anions were obtained. Different variables affecting the reactions were studied and optimized. The formed complexes and the site of interaction were examined by UV-vis, IR, and ^1H NMR techniques, and computational molecular modeling. The formation of the colored complexes were utilized in the development of simple, rapid and accurate spectrophotometric methods for the analysis of LOS-K in pure form as well as in its pharmaceutical tablets. Under the optimum reaction conditions, linear relationships with good correlation coefficients (0.9985-0.9998) were found between the absorbances and the concentrations of LOS-K in the range of 2-200 μg.ml^{-1}. The limits of assays detection ranged from 0.61 to 19.65 μg.ml^{-1}. No interference could be observed from the co-formulated hydrochlorothiazide (HCTZ), as well as from the additives

commonly present in the tablets. The methods were successfully applied to the analysis of tablets from different manufacturers that contain LOS-K, alone or combined with HCTZ, with good accuracy and precision; the recovery percentages ranged from 98.96 ± 1.62% to 101.58 ± 1.29%. The results were compared favourably with the reported method.

Title: Kinetic Spectrophotometric Methods for Determination of Trimetazidine Dihydrochloride

Authors: Ibrahim A. Darwish

Source: *Analytica Chimica Acta, 551, 222-231 (2005)*

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Four simple and sensitive kinetic spectrophotometric methods (I-IV) for the determination of trimetazidine dihydrochloride (TRMZ) have been developed. Method I was based on the oxidation of the drug with alkaline KMn04 producing green manganate species. Method II was based on the formation of colored condensation product between TRMZ and 4-chloro-7-nitrobenzofurazan (NBD-Cl). Method III was based on reaction of TRMZ and with 1,2-naphthoquinone-4-sulphonic acid sodium salt (NQS) forming orange colored product. Method IV was based on the formation of a violet charge-transfer complex between trimetazidine base and p-chloranil (pCL). These reactions were followed spectrophotometrically by measuring the rate of color development at 610, 475, 485 and 560 nm for the reactions with $KMnO_4$, NBD-C1, NQS, and pCL, respectively. The variables affecting the reactions were carefully investigated and the conditions were optimized. The stoichiometries of the reactions were determined, and the reactions pathways were postulated. The initial rate and fixed time methods were utilized for constructing the calibration graphs for the determination of TRMZ concentration. The assays limits of detection were 0.2-2.5 $\mu g.ml^{-1}$. The analytical performance of the methods, in

terms of accuracy and precision, were statistically validated; the results were satisfactory. The methods have been successfully applied to the determination of TRMZ in commercial pharmaceutical formulations. Statistical comparison of the results with the reference method showed excellent agreement and proved that no significant difference in the accuracy and precision.

Title: Validated Spectrphotometric and Fluorimetric Methods for Analysis of Clozapine in Tablets and Urine

Authors: Ibrahim Darwish, Hanaa Abdel-Wadood, Niveen Abdel-Latif

Source: *Annali di Chimica, 95, 345 (2005)*

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

Five spectrophotometric methods and one fluorimetric method have been developed and validated for the analysis of clozapine. The spectrophotometric methods were based on the charge-transfer complexation reaction between clozapine as electron donor and each of iodine as σ-acceptor or 7,7,8,8-tetracyanoquinondimethane (TCNQ), 2,3-dichloro-5,6-dicyano-1,4-benzo-quinone (DDQ), tetracyanoethame (TCNE), and p-chloranilic acid (pCA) as π-acceptors. The obtained complexes were measured spectrophotometrically at 365, 843, 460, 414 and 520 nm for iodine, TCNQ, DDQ, TCNE and pCA respectively. The fluorimetric method was based on the oxidation of clozapine in the presence of perchloric acid by cerium (IV),and subsequent measuring the fluorescence of the produced cerium (III) fluorimetrically at $\lambda_{excitation}$ 260 and $\lambda_{emission}$ 355 nm. Under the optimum assay conditions, Beer's law was obeyed at concentrations ranged from 4-200 μg mL^{-1} for the spectrophotometric methods and from 24-250 ng mL^{-1} for the fluorimetric method. The limits of detection for the spectrophotometric methods were 1.12, 1.76, 2.22, 0.95 and 13.26 μg mL^{-1} for

iodine, TCNQ, DDQ, TCNE and pCA respectively. The limit of detection for the fluorimetric method was 6.69 ng mL^{-1}. The proposed methods were successfully applied to the analysis of clozapine in tablets with good recoveries. The fluorimetric method could also be applied to the analysis of clozapine in spiked urine samples. The molar ratios and the reaction mechanisms were investigated.

Title: Simple Fluorimetric Method for Determination of Certain Antiviral Drugs Via Their Oxidation With Cerium (IV)

Authors: Ibrahim A. Darwish[1], Alaa S. Khedr[1], Hassan F. Askal[1], Ramadan M. Mahmoud[2]

Source: *IL Farmaco, 60, 555-562 (2005)*

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A simple and sensitive fluorimetric method for determination of antiviral drugs: ribavirin, acyclovir, and amantadine hydrochloride has been developed. The method was based on the oxidation of these drugs by cerium (IV) in presence of perchloric acid and subsequent monitoring the fluorescence of the induced cerium (III) at $\lambda_{excitation}$ *255 and* $\lambda_{emission}$ *355 nm. Different variables affecting the reaction conditions such as the concentrations of cerium (IV), type and concentration of acid medium, reaction time, temperature, and the diluting solvents were carefully studied and optimized. Under the optimum conditions, linear relationships with good correlation coefficients (0.9978-0.9996) were found between the relative fluorescence intensity and the concentrations of the investigated drugs in the range of 50-1400 ng* ml^{-1}*. The assay limits of detection and quantitation were 20-49, and 62-160 ng* ml^{-1}*, respectively. The precision of the method was satisfactory; the values of relative standard deviations did not*

exceed 1.58%. No interference could be observed from the excipients commonly present in dosage forms. The proposed method was successfully applied to the analysis of the investigated drugs in pure and pharmaceutical dosage forms with good accuracy and precision; the recovery percentages ranged from 99.2 to 101.2 ± 0.48-1.30%. The results obtained by the proposed fluorimetric method were comparable with those obtained by the official method stated in the United States Pharmacopoeia.

Title: A Validated Spectrfluorimetric Method for Determination of Some Psychoactive Drugs

Authors: Fardous A. Mohamed, Horria A. Mohamed, Samiha A. Hussein, Sameh A. Ahmed

Source: *Journal of Pharmaceutical and Biomedical Analysis, 39, 139-146 (2005)*

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Five psychoactive drugs namely, chlorpromazine HCl. Thioridazime HCl. Clomipramine HCl. Imipramine HCl and desipramine HCl were analyzed by a simple spectrofluorimetric method. The method is based on oxidation of the studied drugs using cerium (IV) in presence of sulphuric acid and monitoring the fluorescence of the formed ceriuim (III) at $\lambda_{excitation}$ *254 and* $\lambda_{emission}$ *355 nm. All variables affecting the reaction conditions such as; cerium (IV) concentration, sulphuric acid concentration, heating time, temperature and dilution solvents were carefully studied. The effect of potential interference due to common ingredients as glucose, sucrose, lactose, citric acid and propylene glycol were investigated. A validation study of the proposed method was carried out according to USP 2002. Beer's law was obeyed for all the studied drugs in the concentration range of 0.05-1.3 µg/ml. Limits of detection range was 0.035-0.038 µg/ml and limits of quantitation of 0.116-0.125 µg/ml were obtained. The method was successfully applied for the assay of the studied drugs in pure form and in pharmaceutical dosage form. Results were compared with official methods.*

The t- and F- values were calculated and compared with the theoretical values, which indicate high accuracy and good precision of the proposed method.

Analytical Chemistry

Title: Monoclonal Antibodies that Exhibit Allosteric Binding Behavior

Authors: Robert C. Blake II[1], Naoya Ohmura[3], Steve J. Lackie[4], Xia Li[2], James B. Delehanty[2,5], Ibrahim A. Darwish[2,6], Diane A. Blake[2]

Source: *Nova Biomedical, 1-36 (2005)*

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Detailed equilibrium binding studies were conducted on 14 monoclonal antibodies that exhibited allosteric binding behavior. When one of the two antigen binding sites on each of these antibodies was occupied with bound antigen, the affinity of the remaining site for antigen appeared to increase. Depending on the identity of the antigen-antibody pair. the extent of this increase in affinity varied from 2.5-(sex hormone binding globulin) to 540-fold (Staphlococcal enterotoxin B). Antibody 8A11, directed toward an epitope

comprised of chelated uranium (VI), exhibited positive cooperativity with respect to antigen binding only when 8A11 was covalently modified with amine-reactive fluorescent dyes. Three antibodies directed toward highly charged metal-free chelators displayed an extreme form of positive cooperativity that was characterized by sigmoidal binding curves that fit the Hill equation with coefficients of 3.7 to 6.5. These latter observations were interpreted in terms of a model in which (i) the anionic chelators bind both to the antigen binding sites and to multiple charged sites on the surface of the compact immunoglobulin, and (ii) the bound, highly charged ligands interact in a complicated fashion through the apolar core of the protein. Three other antibodies exhibited heterotropic cooperativity where the presence of a molecule unrelated to the antigen served to alter the antibody's affinity for the antigen. Goat anti-mouse Fc antibodies and protein G were positive and negative allosteric effectors, respectively, for the binding of chelated uranium to SA II covalently conjugated with indodicarbocyanine (Cy5). In addition to decreasing the affinity of the 8A 11-Cy5 conjugate for chelaled uranium by as much as 4-fold, high concentrations of protein G also altered the nature of the antigen binding curves from sigmoidal to hyperbolic. The presence of high concentrations of antigen decreased the affinity of 8A11-Cy5 for protein G by 20˙ fold. These complex binding data were interpreted in terms of a free energy binding model in which (i) two moles of antigen and one mole of protein G bind to each mole of the 8A11-Cy5 conjugate, (ii) the two moles of antigen promote each other's binding to the antibody, and (iii) the antigen and the protein G oppose each other's binding to the antibody. This is the first detailed description of the energetic balance of reciprocal binding events among the antigen binding sites and distant points on the constant portion of an immunoglobulin.

Title: Chemometrics Assisted Spectrophotometric Method for Simultaneous Determination of Certain Fluoroquinolones and their Decarboxylated Degradants

Authors: A. I. Mohamed[1*], N. A. El-Koussi[2], N. A. Mohamed[1]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 191-198 (2005)*

Address: [1]Department of Pharmaceutical Analytical Chemistry and [2]Department of Pharmaceutical Medicinal Chemistry, Faculty of Pharmacy, Assiut University, Assiut, 71526 Egypt

Simple multivariate spectrophotometric procedure for simultaneous determination of levofloxacin and norfloxacin as representative examples of fluoroquinolones and their decarboxylated degradation products is described. The method is based on the spectrophotometric measurements of the studied drugs and their degradants in 0.1 M hydrochloric acid solutions in the general range of 200-370 nm together with multivariate calibration analysis. The components of mixtures composed of either levofloxacin or norfloxacin and the corresponding degradant. show a considerable degree of spectral overlapping (85.1-87.4%). Resolution of the binary mixtures under investigation has been accomplished mainly by using classical least squares (CLS) analysis. The method is applied successfully for determination of each drug in pure form, laboratory prepared degraded samples and in expired commercial dosage forms and good recoveries were obtained. Results were compared to those obtained by reported procedures for the same combinations and the required statistical parameters were calculated. The degradation rates for the studied drugs at 150° in 2 M HCl were also studied using the proposed procedure. The calculated first order rate constants for the

decarboxylation of the studied drugs were found 0.109 and 0.082 hour^{-1} and the $t_{1/2}$ were 6.32 and 8.50 hours for levofloxacin and norfloxacin respectively.

Analytical Chemistry

Title: Oxidized Diphenylamine as a Spectrophotometric Reagent for the Determination of Some Pharmaceutical Thiols and Thioamides

Authors: K. M. Emara[1], I. H. Refaat[1*], H. M. Abdel-Wadood[1], M. G. Hassan[2]

Source: *Bull. Pharm. Sci., Assiut University, 28 (2), 225-236 (2005)*

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Oxidized diphenylamine is newly utilized as a redox spectrophotometric reagent for the determination of six pharmaceutically important thiol and thioamide drugs named: acetylcystiene, captopril, carbimazole, propylthiouracil, thiopental sodium, and tiopronin. The method is based on measurement of the decrease in absorption intensity of the oxidized diphenylamine (diphenylbenzidine violet, λ_{max}= 580 nm) reagent as a result of the reduction effect of the analysed drugs. This reagent was instantaneously prepared by the oxidation of diphenylamine using ferric sulphate in sulphuric acid medium. The molar ratio of the chromogen reagent was determined to be 2:1; diphenylamine : iron (III). The decrease in colour intensity was found to be quantitatively dependant on drug concentration. Experimental variables including reagent concentration, acid type and concentration, dilution solvent, reaction time, temperature and stability were

studied and optimized. Validation parameters including linearity range, detection and quantitation limits, precision, selectivity and robustness were evaluated. The proposed method was found to be simple, sensitive and accurate one indicated by the studied validation parameters. Good recoveries (98.0±0.14 – 100%, ±0.98) were obtained by the suggested method and it was applied for the determination of the studied drugs in many pharmaceutical dosage forms available in the local market. Good agreement, indicated by acceptable t- & F- tests, was found between results obtained by the suggested method and those obtained by the reported or pharmacopoeial methods.