HerbÃ¢Â€Â“drug interactions: an overview of systematic reviews PubMed Central Posadzki, Paul; Watson, Leala; Ernst, Edzard 2013-01-01 OBJECTIVES The aim of this overview of systematic reviews (SRs) is to evaluate critically the evidence regarding interactions between herbal medicinal products (HMPs) and synthetic drugs. METHODS Four electronic databases were searched to identify relevant SRs. RESULTS FortyÃ¢Â€Â•six SRs of 46 different HMPs met our inclusion criteria. The vast majority of SRs were of poor methodological quality. The majority of these HMPs were not associated with severe herbÃ¢Â€Â“drug interactions. Serious herbÃ¢Â€Â“drug interactions were noted for Hypericum perforatum and Viscum album. The most severe interactions resulted in transplant rejection, delayed emergence from anaesthesia, cardiovascular collapse, renal and liver toxicity, cardiotoxicity, bradycardia, hypovolaemic shock, inflammatory reactions with organ fibrosis and death. Moderately severe interactions were noted for Ginkgo biloba, Panax ginseng, Piper methysticum, Serenoa repens and Camellia sinensis. The most commonly interacting drugs were antiplatelet agents and anticoagulants. CONCLUSION The majority of the HMPs evaluated in SRs were not associated with drug interactions with serious consequences. However, the poor quality and the scarcity of the primary data prevent firm conclusions. PMID:22670731

Modulation of cell surface hydrophobicity and attachment of bacteria to abiotic surfaces and shrimp by Malaysian herb extracts. PubMed Hui, Yew Woh; Dykes, Gary A 2012-08-01 The use of simple crude water extracts of common herbs to reduce bacterial attachment may be a cost-effective way to control bacterial foodborne pathogens, particularly in developing countries. The ability of water extracts of three common Malaysian herbs (Andrographis paniculata, Eurycoma longifolia, and Garcinia atroviridis) to modulate hydrophobicity and attachment to surfaces of five food-related bacterial strains (Bacillus cereus ATCC 14576, Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 10145, Salmonella Enteritidis ATCC 13076, Staphylococcus aureus ATCC 25923) were determined. The bacterial attachment to hydrocarbon assay was used to determine bacterial hydrophobicity. Staining and direct microscopic counts were used to determine attachment of bacteria to glass and stainless steel. Plating on selective media was used to determine attachment of bacteria to shrimp. All extracts were capable of either significantly (P 0.05) to bacterial attachment. For specific combinations of bacteria, surface material, and plant extract, significant correlations (R > 0.80) between hydrophobicity and attachment were observed. The highest of these was observed for S. aureus attachment to stainless steel and glass after treatment with the E. longifolia extract (R = 0.99, P

The use of herbs by california midwives. PubMed Dennehy, Cathi; Tsourounis, Candy; Bui, Lindsey; King, Tekoa L 2010-01-01 To characterize herbal product use (prevalence, types, indications) among Certified Nurse Midwives/Certified Midwives (CNMs/CMs) and Licensed Midwives (LMs) practicing in the state of California and to describe formal education related to herbal products received by midwives during midwifery education. Cross-sectional survey/California/Practicing midwives. A list of LMs and CNMs/CMs practicing in California was obtained through the California Medical Board (CMB) and the American College of Nurse Midwives (ACNM), respectively. The survey was mailed to 343 CNMs/CMs (one third of the ACNM mailing list) and 157 LMs (the complete

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CMB mailing list). Of the 500 surveys mailed, 40 were undeliverable, 146 were returned, and 7 were excluded (30% response rate). Of the 139 completed surveys, 58/102 (57%) of CNMs/CMs and 35/37 (95%) of LMs used herbs, and LMs were more comfortable than CNMs/CMs in recommending herbs to their patients. A majority of LMs had >20 hours of midwifery education on herbs whereas a majority of CNMs/CMs received 0 to 5 hours. Some CNMs/CMs indicated that their practice site limited their ability to use herbs. Common conditions in which LMs and CNMs/CMs used herbs were nausea/vomiting (86% vs. 83%), labor induction (89% vs. 58%), and lactation (86% vs. 65%). Specific herbs for all indications are described. Licensed midwives were more likely than CNMs/CMs to use herbs in clinical practice. This trend was likely a reflection of the amount of education devoted to herbs as well as herbal use limitations that may be encountered in institutional facilities. Ã‚Â© 2010 AWHONN, the Association of Women's Health, Obstetric and Neonatal Nurses.

Development of a LC-MS/MS method for simultaneous determination of metoprolol and its metabolites, ÃŽÂ±-hydroxymetoprolol and O-desmethylmetoprolol, in rat plasma: application to the herb-drug interaction study of metoprolol and breviscapine. PubMed Rao, Zhi; Ma, Yan-rong; Qin, Hong-yan; Wang, Ya-feng; Wei, Yu-hui; Zhou, Yan; Zhang, Guo-qiang; Wang, Xing-dong; Wu, Xin-an 2015-09-01 A simple, specific and sensitive LC-MS/MS method was developed and validated for the simultaneous determination of metoprolol (MET), ÃŽÂ±-hydroxymetoprolol (HMT) and O-desmethylmetoprolol (DMT) in rat plasma. The plasma samples were prepared by protein precipitation, then the separation of the analytes was performed on an Agilent HC-C18 column (4.6Ã¢Â€Â‰ÃƒÂ—Ã¢Â€Â‰250Ã¢Â€Â‰mm, 5Ã¢Â€Â‰Ã‚Âµm) at a flow rate of 1.0Ã¢Â€Â‰mL/min, and post-column splitting (1:4) was used to give optimal interface flow rates (0.2Ã¢Â€Â‰mL/min) for MS detection; the total run time was 8.5Ã¢Â€Â‰min. Mass spectrometric detection was achieved using a triple-quadrupole mass spectrometer equipped with an electrospray source interface in positive ionization mode. The method was fully validated in terms of selectivity, linearity, accuracy, precision, stability, matrix effect and recovery over a concentration range of 3.42-7000Ã¢Â€Â‰ng/mL for MET, 2.05-4200Ã¢Â€Â‰ng/mL for HMT and 1.95-4000Ã¢Â€Â‰ng/mL for DMT. The analytical method was successfully applied to herb-drug interaction study of MET and breviscapine after administration of breviscapine (12.5Ã¢Â€Â‰mg/kg) and MET (40Ã¢Â€Â‰mg/kg). The results suggested that breviscapine have negligible effect on pharmacokinetics of MET in rats; the information may be beneficial for the application of breviscapine in combination with MET in clinical therapy. Copyright Ã‚Â© 2015 John Wiley & Sons, Ltd.

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Synergistic antinociceptive interaction of Syzygium aromaticum or Rosmarinus officinalis coadministered with ketorolac in rats. PubMed BeltrÃƒÂ¡n-Villalobos, Karla Lyzet; DÃƒÂ©ciga-Campos, Myrna; Aguilar-Mariscal, Hidemi; GonzÃƒÂ¡lez-Trujano, MarÃƒÂ-a Eva; MartÃƒÂ-nez-Salazar, MarÃƒÂ-a Fernanda; RamÃƒÂ-rez-Cisneros, MarÃƒÂ-a de Los ÃƒÂ•ngeles; Rios, MarÃƒÂ-a Yolanda; LÃƒÂ³pez-MuÃƒÂ±oz, Francisco Javier 2017-10-01 Syzygium aromaticum (L.) Merr. & L.M. Perry (Mirtaceae) and Rosmarinus officinalis L. (Lamiaceae) are both medicinal plants used for centuries to alleviate pain. The aim of the study was to demonstrate the therapeutic potential utility of herb-drug association of S. aromaticum essential oil or R. officinalis ethanolic extract coadministered with ketorolac. Antinociceptive pharmacological interaction was investigated by an isbolographic study using the formalin test in rats. Both alone and in combination with ketorolac; S. aromaticum and R. officinalis produced a dose-dependent antinociceptive response. To plot the isobologram, we used the effective dose 50 of each one component in a fixed 1:1 ratio. The isobolographic analysis showed that, in both combinations, ketorolac plus essential oil S. aromaticum and ketorolac plus ethanolic extract R. officinalis, the experimental value (Z exp) was lower than the theoretical value (Z add). In addition, this study shows that eugenol, a metabolite present in S. aromaticum, and ursolic acid, a metabolite present in R. officinalis, also synergized the antinociceptive effect of ketorolac. While, the oleanolic acid present in both medicinal species did not show a synergistic antinociceptive effect in combination with ketorolac. No adverse effects were observed with these herb-drug interactions. These findings suggest that essential oil S. aromaticum and ethanolic extract R. officinalis could be useful in combination with ketorolac for the treatment of inflammatory pain. Copyright Ã‚Â© 2017 Elsevier Masson SAS. All rights reserved.

Drug membrane interaction and the importance for drug transport, distribution, accumulation, efficacy and resistance. PubMed Seydel, J K; Coats, E A; Cordes, H P; Wiese, M 1994-10-01 Some aspects of drug membrane interaction and its influence on drug transport, accumulation, efficacy and resistance have been discussed. The interactions manifest themselves macroscopically in changes in the physical and thermodynamic properties of "pure membranes" or bilayers. As various amounts of foreign molecules enter the membrane, in particular the main gel to liquid crystalline phase transition can be dramatically changed. This may change permeability, cell-fusion, cell resistance and may also lead to changes in conformation of the embedded receptor proteins. Furthermore, specific interactions with lipids may lead to drug accumulation in membranes and thus to much larger concentrations at the active site than present in the surrounding water phase. The lipid environment may also lead to changes in the preferred conformation of drug molecules. These events are directly related to drug efficacy. The determination of essential molecular criteria for the interaction could be used to design new and more selective therapeutics. This excursion in some aspects of drug membrane interaction underlines the importance of lipids and their interaction with drug molecules for our

understanding of drug action, but this is not really a new thought but has been formulated in 1884 by THUDICUM: "Phospholipids are the centre, life and chemical soul of all bioplasm whatsoever, that of plants as well as of animals".

Pharmacokinetic Interactions between Drugs and Botanical Dietary Supplements PubMed Central Sprouse, Alyssa A. 2016-01-01 The use of botanical dietary supplements has grown steadily over the last 20 years despite incomplete information regarding active constituents, mechanisms of action, efficacy, and safety. An important but underinvestigated safety concern is the potential for popular botanical dietary supplements to interfere with the absorption, transport, and/or metabolism of pharmaceutical agents. Clinical trials of drugÃ¢Â€Â“botanical interactions are the gold standard and are usually carried out only when indicated by unexpected consumer side effects or, preferably, by predictive preclinical studies. For example, phase 1 clinical trials have confirmed preclinical studies and clinical case reports that St. JohnÃ¢Â€Â™s wort (Hypericum perforatum) induces CYP3A4/CYP3A5. However, clinical studies of most botanicals that were predicted to interact with drugs have shown no clinically significant effects. For example, clinical trials did not substantiate preclinical predictions that milk thistle (Silybum marianum) would inhibit CYP1A2, CYP2C9, CYP2D6, CYP2E1, and/or CYP3A4. Here, we highlight discrepancies between preclinical and clinical data concerning drugÃ¢Â€Â“botanical interactions and critically evaluate why some preclinical models perform better than others in predicting the potential for drugÃ¢Â€Â“botanical interactions. Gaps in knowledge are also highlighted for the potential of some popular botanical dietary supplements to interact with therapeutic agents with respect to absorption, transport, and metabolism. PMID:26438626

Position-aware deep multi-task learning for drug-drug interaction extraction. PubMed Zhou, Deyu; Miao, Lei; He, Yulan 2018-05-01 A drug-drug interaction (DDI) is a situation in which a drug affects the activity of another drug synergistically or antagonistically when being administered together. The information of DDIs is crucial for healthcare professionals to prevent adverse drug events. Although some known DDIs can be found in purposely-built databases such as DrugBank, most information is still buried in scientific publications. Therefore, automatically extracting DDIs from biomedical texts is sorely needed. In this paper, we propose a novel position-aware deep multi-task learning approach for extracting DDIs from biomedical texts. In particular, sentences are represented as a sequence of word embeddings and position embeddings. An attention-based bidirectional long short-term memory (BiLSTM) network is used to encode each sentence. The relative position information of words with the target drugs in text is combined with the hidden states of BiLSTM to generate the position-aware attention weights. Moreover, the tasks of predicting whether or not two drugs interact with each other and further distinguishing the types of interactions are

learned jointly in multi-task learning framework. The proposed approach has been evaluated on the DDIExtraction challenge 2013 corpus and the results show that with the position-aware attention only, our proposed approach outperforms the state-of-the-art method by 0.99% for binary DDI classification, and with both position-aware attention and multi-task learning, our approach achieves a micro F-score of 72.99% on interaction type identification, outperforming the state-of-the-art approach by 1.51%, which demonstrates the effectiveness of the proposed approach.

Warfarin-drug interactions: An emphasis on influence of polypharmacy and high doses of amoxicillin/clavulanate. PubMed Abdel-Aziz, Mahmoud I; Ali, Mostafa A Sayed; Hassan, Ayman K M; Elfaham, Tahani H 2016-01-01 The objective of this study was to investigate the effect of polypharmacy and high doses of amoxicillin/clavulanate on warfarin response in hospitalized patients. This was a prospective cross-sectional observational study on 120 patients from July 2013 to January 2014. Potentially interacting drugs were classified according to their tendency of increasing international normalized ratio (INR) or bleeding risk. The 87.5% of patients prescribed high-dose amoxicillin/clavulanate (10-12 g daily) compared with 28.9% of patients prescribed a normal dose (up to 3.6 g daily) had INR values Ã¢Â‰Â¥ 4 during the hospital stay (P Ã¢Â‰Â¤ .001). Increased number of potentially interacting drugs that are known to increase INR was a significant predictor of having INR values Ã¢Â‰Â¥ 4 (OR, 2.5; 95%CI, 1.3-4.7), and increased number of potentially interacting drugs that are known to increase bleeding risk was a significant predictor of experiencing bleeding episodes (OR, 3.1; 95%CI, 1.3-7.3). High doses of amoxicillin/clavulanate were associated with a higher risk of over-anticoagulation when combined with warfarin than were normal doses. Increased risk of having INR Ã¢Â‰Â¥ 4 and bleeding events was associated with increased numbers of potentially interacting drugs prescribed, indicating that polypharmacy is a problem of concern. Frequent monitoring of warfarin therapy along with patients' medications is necessary to avoid complications.

HERB: A production system for programming with hierarchical expert rule bases: User's manual, HERB Version 1. 0 DOE Office of Scientific and Technical Information (OSTI.GOV) Hummel, K.E. 1987-12-01 Expert systems are artificial intelligence programs that solve problems requiring large amounts of heuristic knowledge, based on years of experience and tradition. Production systems are domain-independent tools that support the development of rule-based expert systems. This document describes a general purpose production system known as HERB. This system was developed to support the programming of expert systems using hierarchically structured rule bases. HERB encourages the partitioning of rules into multiple rule bases and supports the use of multiple conflict resolution strategies. Multiple rule bases can also be placed on a system stack and simultaneously searched during each interpreter cycle. BothmoreÃ, Ã,Â»

backward and forward chaining rules are supported by HERB. The condition portion of each rule can contain both patterns, which are matched with facts in a data base, and LISP expressions, which are explicitly evaluated in the LISP environment. Properties of objects can also be stored in the HERB data base and referenced within the scope of each rule. This document serves both as an introduction to the principles of LISP-based production systems and as a user's manual for the HERB system. 6 refs., 17 figs.Ã‚Â«Ã‚ less

Predicting drug-target interactions using restricted Boltzmann machines. PubMed Wang, Yuhao; Zeng, Jianyang 2013-07-01 In silico prediction of drug-target interactions plays an important role toward identifying and developing new uses of existing or abandoned drugs. Network-based approaches have recently become a popular tool for discovering new drug-target interactions (DTIs). Unfortunately, most of these network-based approaches can only predict binary interactions between drugs and targets, and information about different types of interactions has not been well exploited for DTI prediction in previous studies. On the other hand, incorporating additional information about drug-target relationships or drug modes of action can improve prediction of DTIs. Furthermore, the predicted types of DTIs can broaden our understanding about the molecular basis of drug action. We propose a first machine learning approach to integrate multiple types of DTIs and predict unknown drug-target relationships or drug modes of action. We cast the new DTI prediction problem into a two-layer graphical model, called restricted Boltzmann machine, and apply a practical learning algorithm to train our model and make predictions. Tests on two public databases show that our restricted Boltzmann machine model can effectively capture the latent features of a DTI network and achieve excellent performance on predicting different types of DTIs, with the area under precision-recall curve up to 89.6. In addition, we demonstrate that integrating multiple types of DTIs can significantly outperform other predictions either by simply mixing multiple types of interactions without distinction or using only a single interaction type. Further tests show that our approach can infer a high fraction of novel DTIs that has been validated by known experiments in the literature or other databases. These results indicate that our approach can have highly practical relevance to DTI prediction and drug repositioning, and hence advance the drug discovery process. Software and datasets are available on request. Supplementary data are

Drug-drug interaction and doping: Effect of non-prohibited drugs on the urinary excretion profile of methandienone. PubMed Mazzarino, Monica; KhevenhÃƒÂ¼ller-Metsch, Franziska L; Fiacco, Ilaria; Parr, Maria Kristina; de la Torre, Xavier; BotrÃƒÂ¨, Francesco 2018-05-15 The potential consequences of drug-drug interactions on the excretion profile of the anabolic androgenic steroid methandienone (17ÃŽÂ²-hydroxy-17ÃŽÂ±-methylandrosta-1,4-dien-3-one) are discussed here. More specifically, we have evaluated by in vitro and in vivo experiments the effects of seven non-prohibited

drugs (fluconazole, ketoconazole, itraconazole, miconazole, fluoxetine, paroxetine and nefazodone) on the main metabolic pathways of methandienone. These are selected among those most commonly used by the athletes. The in vitro assays were based on the use of human liver microsomes, specific recombinant enzyme isoforms of cytochrome P450 and uridine 5'-diphospho-glucuronosyl-transferase. The in vivo study was performed by analyzing urines collected after the oral administration of methandienone with and without the co-administration of ketoconazole. Methandienone and its metabolites were determined by liquid chromatography-mass spectrometry-based techniques after sample pre-treatment including an enzymatic hydrolysis step (performed only for the investigation on phase II metabolism) and liquid/liquid extraction with t-butyl methyl-ether. The results from the in vitro experiments showed that the formation of the hydroxylated and dehydrogenated metabolites was significantly reduced in the presence of itraconazole, ketoconazole, miconazole and nefazodone, whereas the production of the 18-nor-hydroxylated metabolites and glucuronidation reactions was reduced significantly only in the presence of ketoconazole and miconazole. The analysis of the post-administration samples confirmed the in vitro observations, validating the hypothesis that drug-drug interaction may cause significant alterations in the metabolic profile of banned drugs, making their detection during doping control tests more challenging.

Acaricide, Fungicide and Drug Interactions in Honey Bees (Apis mellifera) PubMed Central Johnson, Reed M.; Dahlgren, Lizette; Siegfried, Blair D.; Ellis, Marion D. 2013-01-01 Background Chemical analysis shows that honey bees (Apis mellifera) and hive products contain many pesticides derived from various sources. The most abundant pesticides are acaricides applied by beekeepers to control Varroa destructor. Beekeepers also apply antimicrobial drugs to control bacterial and microsporidial diseases. Fungicides may enter the hive when applied to nearby flowering crops. Acaricides, antimicrobial drugs and fungicides are not highly toxic to bees alone, but in combination there is potential for heightened toxicity due to interactive effects. Methodology/Principal Findings Laboratory bioassays based on mortality rates in adult worker bees demonstrated interactive effects among acaricides, as well as between acaricides and antimicrobial drugs and between acaricides and fungicides. Toxicity of the acaricide tau-fluvalinate increased in combination with other acaricides and most other compounds tested (15 of 17) while amitraz toxicity was mostly unchanged (1 of 15). The sterol biosynthesis inhibiting (SBI) fungicide prochloraz elevated the toxicity of the acaricides tau-fluvalinate, coumaphos and fenpyroximate, likely through inhibition of detoxicative cytochrome P450 monooxygenase activity. Four other SBI fungicides increased the toxicity of tau-fluvalinate in a dose-dependent manner, although possible evidence of P450 induction was observed at the lowest fungicide doses. Non-transitive interactions between some acaricides were observed. Sublethal amitraz pre-treatment increased the toxicity of the three P450-detoxified acaricides, but amitraz toxicity was not changed by sublethal treatment with the same three

acaricides. A two-fold change in the toxicity of tau-fluvalinate was observed between years, suggesting a possible change in the genetic composition of the bees tested. Conclusions/Significance Interactions with acaricides in honey bees are similar to drug interactions in other animals in that P450-mediated detoxication appears to play an

Interaction Between Low-Dose Methotrexate and Nonsteroidal Anti-inflammatory Drugs, Penicillins, and Proton Pump Inhibitors. PubMed Hall, Jill J; Bolina, Monika; Chatterley, Trish; Jamali, Fakhreddin 2017-02-01 To review the potential drug interactions between low-dose methotrexate (LD-MTX) and nonsteroidal anti-inflammatory drugs (NSAIDs), penicillins, and proton-pump inhibitors (PPIs) given the disparity between interactions reported for high-dose and low-dose MTX to help guide clinicians. A literature search was performed in MEDLINE (1946 to September 2016), EMBASE (1974 to September 2016), and International Pharmaceutical Abstracts (1970 to January 2015) to identify reports describing potential drug interactions between LD-MTX and NSAIDS, penicillins, or PPIs. Reference lists of included articles were reviewed to find additional eligible articles. All English-language observational, randomized, and pharmacokinetic (PK) studies assessing LD-MTX interactions in humans were analyzed to determine clinical relevance in making recommendations to clinicians. Clinical case reports were assigned a Drug Interaction Probability Scale score. A total of 32 articles were included (28 with NSAIDs, 3 with penicillins, and 2 with PPIs [1 including both PPI and NSAID]). Although there are some PK data to describe increased LD-MTX concentrations when NSAIDs are used concomitantly, the clinical relevance remains unclear. Based on the limited data on LD-MTX with penicillins and PPIs, no clinically meaningful interaction was identified. Given the available evidence, the clinical importance of the interaction between LD-MTX and NSAIDs, penicillins, and PPIs cannot be substantiated. Health care providers should assess the benefit and risk of LD-MTX regardless of concomitant drug use, including factors known to predispose patients to MTX toxicity, and continue to monitor clinical and laboratory parameters per guideline recommendations.

A Review of the Toxicity of HIV Medications II: Interactions with Drugs and Complementary and Alternative Medicine Products. PubMed Stolbach, Andrew; Paziana, Karolina; Heverling, Harry; Pham, Paul 2015-09-01 For many patients today, HIV has become a chronic disease. For those patients who have access to and adhere to lifelong antiretroviral (ARV) therapy, the potential for drug-drug interactions has become a real and life-threatening concern. It is known that most ARV drug interactions occur through the cytochrome P450 (CYP) pathway. Medications for comorbid medical conditions, holistic supplements, and illicit drugs can be affected by CYP inhibitors and inducers and have the potential to cause harm and toxicity. Protease inhibitors (PIs) tend to inhibit CYP3A4, while most non-nucleoside reverse transcriptase inhibitors (NNRTIs) tend to induce the enzyme. As such, failure to adjust the dose of co-administered medications, such as statins and steroids, may lead to serious complications including rhabdomyolysis

and hypercortisolism, respectively. Similarly, gastric acid blockers can decrease several ARV absorption, and warfarin doses may need to be adjusted to maintain therapeutic concentrations. Illicit drugs such as methylenedioxymethamphetamine (MDMA, "ecstasy") in combination with PIs lead to increased toxicity, while the concomitant administration of sedative drugs such as midazolam and alprazolam in patients taking PIs can result in prolonged sedation, delayed recovery, and increased length of stay. Even supplements like St. John's Wort can alter PI concentrations. In theory, any drug that is metabolized by CYP has potential for a pharmacokinetic drug-drug interaction with all PIs, cobicistat, and most NNRTIs. When adding a new medication to an ARV regimen, use of a drug-drug interaction software and/or consultation with a clinical pharmacist/pharmacologist or HIV specialist is recommended.

Drug-drug interactions between immunosuppressants and antidiabetic drugs in the treatment of post-transplant diabetes mellitus. PubMed Vanhove, Thomas; Remijsen, Quinten; Kuypers, Dirk; Gillard, Pieter 2017-04-01 Post-transplant diabetes mellitus is a frequent complication of solid organ transplantation that generally requires treatment with lifestyle interventions and antidiabetic medication. A number of demonstrated and potential pharmacokinetic drug-drug interactions (DDIs) exist between commonly used immunosuppressants and antidiabetic drugs, which are comprehensively summarized in this review. Cyclosporine (CsA) itself inhibits the cytochrome P450 (CYP) 3A4 enzyme and a variety of drug transporters. As a result, it increases exposure to repaglinide and sitagliptin, will likely increase the exposure to nateglinide, glyburide, saxagliptin, vildagliptin and alogliptin, and could theoretically increase the exposure to gliquidone and several sodium-glucose transporter (SGLT)-2 inhibitors. Currently available data, although limited, suggest that these increases are modest and, particularly with regard to gliptins and SGLT-2 inhibitors, unlikely to result in hypoglycemia. The interaction with repaglinide is more pronounced but does not preclude concomitant use if repaglinide dose is gradually titrated. Mycophenolate mofetil and azathioprine do not engage in DDIs with any antidiabetic drug. Although calcineurin inhibitors (CNIs) and mammalian target of rapamycin inhibitors (mTORi) are intrinsically prone to DDIs, their disposition is not influenced by metformin, pioglitazone, sulfonylureas (except possibly glyburide) or insulin. An effect of gliptins on the disposition of CNIs and mTORi is unlikely, but has not been definitively ruled out. Based on their disposition profiles, glyburide and canagliflozin could affect CNI and mTORi disposition although this requires further study. Finally, delayed gastric emptying as a result of glucagon-like peptide-1 agonists seems to have a limited, but not necessarily negligible effect on CNI disposition.

Predicting drug-target interaction for new drugs using enhanced similarity measures and super-target clustering.

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PubMed Shi, Jian-Yu; Yiu, Siu-Ming; Li, Yiming; Leung, Henry C M; Chin, Francis Y L 2015-07-15 Predicting drug-target interaction using computational approaches is an important step in drug discovery and repositioning. To predict whether there will be an interaction between a drug and a target, most existing methods identify similar drugs and targets in the database. The prediction is then made based on the known interactions of these drugs and targets. This idea is promising. However, there are two shortcomings that have not yet been addressed appropriately. Firstly, most of the methods only use 2D chemical structures and protein sequences to measure the similarity of drugs and targets respectively. However, this information may not fully capture the characteristics determining whether a drug will interact with a target. Secondly, there are very few known interactions, i.e. many interactions are "missing" in the database. Existing approaches are biased towards known interactions and have no good solutions to handle possibly missing interactions which affect the accuracy of the prediction. In this paper, we enhance the similarity measures to include non-structural (and non-sequence-based) information and introduce the concept of a "super-target" to handle the problem of possibly missing interactions. Based on evaluations on real data, we show that our similarity measure is better than the existing measures and our approach is able to achieve higher accuracy than the two best existing algorithms, WNN-GIP and KBMF2K. Our approach is available at http://web.hku.hk/Ã¢Â^Â¼liym1018/projects/drug/drug.html or http://www.bmlnwpu.org/us/tools/PredictingDTI_S2/METHODS.html. Copyright Ã,Â© 2015 Elsevier Inc. All rights reserved.

The role of drug profiles as similarity metrics: applications to repurposing, adverse effects detection and drug-drug interactions. PubMed Vilar, Santiago; Hripcsak, George 2017-07-01 Explosion of the availability of big data sources along with the development in computational methods provides a useful framework to study drugs' actions, such as interactions with pharmacological targets and off-targets. Databases related to protein interactions, adverse effects and genomic profiles are available to be used for the construction of computational models. In this article, we focus on the description of biological profiles for drugs that can be used as a system to compare similarity and create methods to predict and analyze drugs' actions. We highlight profiles constructed with different biological data, such as target-protein interactions, gene expression measurements, adverse effects and disease profiles. We focus on the discovery of new targets or pathways for drugs already in the pharmaceutical market, also called drug repurposing, in the interaction with off-targets responsible for adverse reactions and in drug-drug interaction analysis. The current and future applications, strengths and challenges facing all these methods are also discussed. Biological profiles or signatures are an important source of data generation to deeply analyze biological actions with important implications in drug-related studies. Ã,Â© The Author 2016. Published by Oxford University Press. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

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Concurrent Use of Hypnotic Drugs and Chinese Herbal Medicine Therapies among Taiwanese Adults with Insomnia Symptoms: A Population-Based Study. PubMed Lee, Kuei-Hua; Tsai, Yueh-Ting; Lai, Jung-Nien; Lin, Shun-Ku 2013-01-01 Background. The increased practice of traditional Chinese medicine (TCM) worldwide has raised concerns regarding herb-drug interactions. The purpose of our study is to analyze the concurrent use of Chinese herbal products (CHPs) among Taiwanese insomnia patients taking hypnotic drugs. Methods. The usage, frequency of services, and CHP prescribed among 53,949 insomnia sufferers were evaluated from a random sample of 1 million beneficiaries in the National Health Insurance Research Database. A logistic regression method was used to identify the factors that were associated with the coprescription of a CHP and a hypnotic drug. Cox proportional hazards regressions were performed to calculate the hazard ratios (HRs) of hip fracture between the two groups. Results. More than 1 of every 3 hypnotic users also used a CHP concurrently. Jia-Wei-Xiao-Yao-San (Augmented Rambling Powder) and Suan-Zao-Ren-Tang (Zizyphus Combination) were the 2 most commonly used CHPs that were coadministered with hypnotic drugs. The HR of hip fracture for hypnotic-drug users who used a CHP concurrently was 0.57-fold (95% CI = 0.47-0.69) that of hypnotic-drug users who did not use a CHP. Conclusion. Exploring potential CHP-drug interactions and integrating both healthcare approaches might be beneficial for the overall health and quality of life of insomnia sufferers.

Reference

Strategies and Tactics of Behavioral Research and Practice

Critical Thinking in Clinical Research: Applied Theory and Practice Using Case Studies