AGFD 76 Effect of selected phytochemicals on cell proliferation in A549 nonsmall cell lung cancer cells Hyungeun Yoon, HY65@cornell.edu, Food Science and Technology, Cornell University, 630 W North Street, Geneva, NY 14456, and C. Y. Lee, cyl1@cornell.edu, Dept. Food Sci. & Tech, Cornell University, Food Research Lab, Geneva, NY The effects of quercetin 3-beta-D-glucoside, resveratrol, and curcumin on A549 lung cancer cell proliferation and the mechanism of these phytochemicals in regulating apoptosis and cell cycle arrest were investigated. The cells were treated with three compounds and cell viability was measured with MTT assay. After 24 hour incubation with these phytochemicals, proteins related to apoptosis and cell cycle in A549 cells were quantified with Western blotting method. All three compounds inhibited A549 cell proliferation in a dose-dependent manner. Quercetin significantly decrease the expression level of CDK4 at concentration of 5 micro M and above. Curcumin lowered expression of Bcl-2, cyclin D1, and CDK4 at concentrations of 100 micro M, 50 micro M and above, and 50 micro M and above, respectively. This study shows that some bioactive phytochemicals, which can be obtained from a normal diet, inhibited lung cancer cell proliferation and regulated expression of proteins involved in apoptosis and cell cycle. Therefore, these phytochemicals may be used in anticancer treatment.

AGFD 77 Antioxidant activities of infusions prepared from the Noni plant Brett J West, brett_west@tni.com, Research and Development Dept, Tahitian Noni Int'l, 737 East 1180 South, American Fork, UT Hot water infusions made from various parts of noni (Morinda citrifolia) were used traditionally to promote health. The antioxidant activity of infusions from the noni plant (1 g in 100 mL hot water for 10 min) were determined by the DPPH test (1:1 v/v with 0.4 mM DPPH in EtOH at 37°C for 60 min, abs. at 515 nm) and compared to green tea. DPPH reducing activities were 88% (blossoms), 84% (roasted leaves), 82% (unroasted leaves), 77% (green tea), 57% (bark), 53% (root), and 49% (seeds). During initial in vitro safety tests of noni blossom, the infusion was non-toxic in brine shrimp (LC50>1 mg/ml), and the ethanol extract was not genotoxic in E.coli PQ37 (SOS-Chromotest) up to 5 mg/ml. The entire plant contains antioxidant compounds. The blossom and leaf infusions contain compounds that are more effective in reducing the DPPH radical than those in the green tea infusion.

AGFD 78 Quercetin sulfates/glucuronides exert anti-inflammatory activity on activated macrophages Shih-Hua Fang1, shfang@mail.cmu.edu.tw, Shiuan-Pey Lin2, Yu-Chi Hou3, houyc@mail.cmu.edu.tw, and Pei-Dawn Lee Chao3. (1) Inst. of Athletics, China Medical Univ., Taichung, Taiwan, 16, SEC1, Shuan-Shih Rd, Taichung, Taiwan, (2) Graduate Inst. of Pharmaceutical Chemistry, China Medical Univ., Taichung, Taiwan, Taichung, Taiwan, (3) School of Pharmacy, China Medical Univ., Taichung, Taiwan, Taichung, Taiwan Quercetin glycosides are a class of flavonoids widely distributed in plant foods such as onion, grape, strawberry and grapefruit. Nowadays, quercetin-containing dietary supplements are readily accessible from internet. In recent decade, there is growing evidence showing that quercetin is not present in blood and its conjugated metabolites are predominant. This study prepared the serum metabolites of quercetin to investigate the effects of quercetin sulfates/glucuronides on the production of nitric oxide (NO) and cytokines from lipopolysaccharide-activated macrophages. The results indicated that NO, tumor necrosis factor-$f\tilde{N}fn$nand interleukin-12 productions from activated murine macrophages were inhibited dose-dependently. Furthermore, the soup of the flower buds of Sophora japonica, a food and herb abundant in rutin (quercetin rhamnoside), was given to mice twice daily for two months. The phagocyte activities in the peripheral blood were found significantly decreased. In conclusion, rutin intake might exhibit anti-inflammatory activity through decreasing the functions of macrophages.

AGFD 79 Conjugation of hydroxycinnamic acids by human UDP-glucuronosyltransferases and sulfotransferase in vitro and in vivo Chi Chun Wong1, fsccdw@leeds.ac.uk, Hansruedi Glatt2, glatt@dife.de, Denis Barron3, Denis.Barron@rdls.nestle.com, A Stalmach4, Alan Crozier4, 3, and Gary Williamson5, G.Williamson@leeds.ac.uk. (1) Procter Dept of Food Science, Univ. of Leeds, Leeds, United Kingdom, (2) Department of Nutritional Toxicology, German Institute of Human Nutrition (DIfE) Potsdam-Rehbrücke, Nuthetal, Germany, (3) Nestlé Research Center, Lausanne, Switzerland, (4) 1Plant Products & Human Nutrition Group, Graham Kerr Building, Division of Biochemistry & Molecular Biology, University of Glasgow, Glasgow, G12-8QQ, United Kingdom, (5) University of Leeds, Procter Department of Food Science, leeds, United Kingdom Hydroxycinnamic acids are a class of polyphenolic antioxidants widely found in dietary plants. Phase II metabolism of hydroxycinnamic acids are a major pathway of metabolism affecting biological activities. We evaluated the activities of phase II enzymes UDP-glucuronosyltransferases (UGTs) and sulfotransferases (SULTs) towards five dietary hydroxycinnamic acids. Analysis of kinetics of hydroxycinnamic acid conjugation in the human liver and intestinal S9 homogenates revealed that sulfation is the major pathway of metabolism. Assessment of activity using SULTs showed that SULT1A1 active in conjugation towards all five phenolic acids. Only isoferulic acid was significantly glucuronidated by human liver S9 homogenates, explained by the high activity of liver-specific UGT1A9 for isoferulic acid. An intervention study in healthy humans found that sulfated conjugates are predominant metabolites the in urine. This implies that the conjugating activity of SULTs have a significant impact on metabolism of hydroxycinnamic acids.

AGFD 80 Marked increase of oral absorption of hesperetin in rats through nanosuspension formation Shang-Yuan Tsai1, sytsai@mail.cmu.edu.tw, Yu-Chi Hou1, houyc@mail.cmu.edu.tw, PDL. Chao1, pdlee@mail.cmu.edu.tw, and Yen-Jen Wang2, sytsai@mail.cmu.edu.tw. (1) Department of Pharmacy, China Medical University, 91 Sheih-Shih Rd., Taichung 40402, Taiwan, (2) Institute of Pharmacy, China Medical University, Taichung 40402 Hesperetin, a citrus flavonoid, has been reported to possess various beneficial bioactivities. The aim of this study was to prepare nanosuspension of hesperetin (NH) to enhance its oral absorption. Solvent-displacement method was used to prepare the nanosuspension formula of NH. The experimental design using L9(34) was conducted for optimizing the formula. The mean particle size of the optimized formula was 80 nm which showed good physical stability. Furthermore, the efficiency of the NH nanosuspension formula was evaluated by comparing the pharmacokinetics of hesperetin and its conjugated metabolites with that of NH solution after administrations of both formulas to rats. The results showed that although the free form of hesperetin was not detected in serum after intake of both formulas, the systemic exposure of NH conjugated metabolites was significantly enhanced when NH was administered in nanosuspension formula.

AGFD 81 Food-drug interaction between licorice and cyclosporine in rats PDL. Chao1, pdlee@mail.cmu.edu.tw, Shiuan-Pey Lin2, Shang-Yuan Tsai1, sytsai@mail.cmu.edu.tw, and Yu-Chi Hou1, houyc@mail.cmu.edu.tw. (1) Dept of Pharmacy, China Medical Univ, 91 Sheih-Shih Rd., Taichung 40402, Taiwan, (2) Graduate Inst. of Pharmaceutical Chemistry, China Medical University Licorice (root of Glycyrrhiza uralensis FISCH) is a worldwide food additive and a popular oriental herb. Licorice and its major constituent glycyrrhizin (GZ) have been reported to inhibit cytochrome-dependent metabolic enzymes and P-glycoprotein (Pgp), an efflux transporter. Cyclosporine, an

important immunosupressant with narrow therapeutic window, is a substrate of CYP3A4 and Pgp. This study investigated the effects of licorice and GZ on the absorption and disposition of cyclosporine. Rats were orally given cyclosporine without and with various dosage regimen of GZ and licorice decoction (LD). The blood concentration of cyclosporine was analyzed by a fluorescence polarization immunoassay. Unexpectedly, the Cmax and AUC0-t of cyclosporine were significantly decreased by coadministration with GZ and LD, indicating that the bioavailability of cyclosporine was greatly reduced. In conclusion, the concurrent use of licorice with cyclosporine should be cautious in order to ensure the efficacy of cyclosporine in transplant patients.

AGFD 82 Miso markedly decreased cyclosporine absorption in rats Yu-Chi Hou1, houyc@mail.cmu.edu.tw, Ying-Chang Chi2, Shang-Yuan Tsai3, sytsai@mail.cmu.edu.tw, and PDL. Chao3, pdlee@mail.cmu.edu.tw. (1) School of Pharmacy, China Medical University, Taichung, Taiwan, 91, Hsueh-Shih Rd, Taichung 40402, Taiwan,, (2) Graduate Institute of Pharmaceutical Chemistry, China Medical University, Taichung 40402, Taiwan, (3) Department of Pharmacy, China Medical University, Taichung 40402, Taiwan Soybean products are widely consumed in Asian countries and provide a major source of isoflavones. Miso, a fermented soy paste, is popularly used for cooking. Cyclosporine, an immunosuppressant with narrow therapeutic index, is a substrate of CYP3A4 and Pgp, an efflux transporter. Isoflavones have been reported to modulate CYP3A4 and Pgp in vitro. This study investigated the effect of miso on the absorption and disposition of cyclosporine. Rats were orally and intravenously administered cyclosporine with and without miso. The results showed that coadministration of miso significantly decreased the Cmax and AUC0-t of oral cyclosporine. When miso was given 1 h before cyclosporine, Cmax and AUC0-t of cyclosporine were also significantly reduced. However, the intravenous pharmcokinetics of cyclosporine was not affected, indicating that this food-drug interaction occurred at the absorption site. In conclusion, miso significantly decreased the absorption of cyclosporine. Patients treated with cyclosporine should be discouraged from taking miso concurrently.

AGFD 83 L-tryptophan as a novel therapeutic agent for chronic gut inflammation Yoshinori Mine, ymine@uoguelph.ca, Connie J. Kim, Jennifer Kovacs-Nolan, jkovacsn@uoguelph.ca, Chengbo Yang, Tania Archbold, and Ming Z. Fan, Univ. of Guelph, Guelph, ON N1G2W1, Canada Conventional therapies for the treatment of inflammatory bowel disease (IBD) have demonstrated limited efficacy and potential toxicity; therefore there is a need for novel therapies. The objective of this study was to assess the therapeutic benefits of tryptophan in a porcine model of dextran sodium sulfate (DSS)-induced colitis. DSS was administered to piglets via intra-gastric catheter for five days at 1.25gDSS/kg body weight (BW) followed by tryptophan administration at 110mg/BW. Supplementation with tryptophan ameliorated clinical symptoms and improved weight gain to feed intake conversion ratios. Histological scores and measurements were also improved and gut permeability was notably reduced in tryptophan supplemented animals. Tryptophan reduced the expression of the pro-inflammatory cytokines tumor necrosis factor, alpha;, interleukin (IL)-6, interferon (IFN)-gamma;, IL-12p40, IL-1 beta;, and IL-17, as well as IL-8 and intracellular adhesion molecule (ICAM)-1. These results suggest that L-tryptophan is a promising novel therapeutic for the treatment of IBD.

AGFD 84 Determination of free trenbolone acetate and its major metabolites in bovine milk by liquid chromatography-tandem mass spectrometry Qingsong Cai, qingsong.cai@tiehh.ttu.edu, Jiafan Wang, jiafan.wang@tiehh.ttu.edu, Randi D. Shannahan, randi.shannahan@ttu.edu, Brett R. Blackwell, brett.blackwell@tiehh.ttu.edu, John M. Brausch, john.brausch@tiehh.ttu.edu, Philip N. Smith, philip.smith@tiehh.ttu.edu, and George P. Cobb, george.cobb@tiehh.ttu.edu, Dept of Environmental Toxicology, The Inst. of Environmental and Human Health, Texas Tech Univ, Box 41163, Lubbock, TX Trenbolone acetate (TBA) is a powerful synthetic anabolic steroid used as a growth promoter in beef cattle. After administration, TBA is rapidly hydrolyzed to 17ß-trenbolone (ß-TBOH), the active form which is further biotransformed to trendione (TBD) and 17a-trenbolone (a-TBOH). Lack of certainty regarding the gestational status of free range cows may result in the inadvertent administration of TBA and other growth promoters. Kinetics studies have confirmed that less than 1% of TBA is excreted via milk in such cases. Enzyme-linked immunoassays have heretofore been used to quantitate TBA and its metabolites in biological matrices; however, the ELISA method is less effective on milk samples due to antibody cross-reactivities. Given the potential endocrine-disrupting capacity of these compounds, a sensitive and reliable analytical method is of great interest in order to assess TBA and metabolite residues in dairy products. Herein, a specific and sensitive method based on liquid chromatography–tandem mass spectrometry using electrospray ionization (LC-ESI-MS/MS) has been developed for the determination of free TBA and its three major metabolites in bovine milk. Norethandrolone was used as internal standard. The sample preparation essentially involved liquid-liquid extraction followed by cleanup on reversed-phase and ion-exchange solid-phase extraction cartridges. The procedure was optimized to obtain maximum recovery and minimum signal suppression/enhancement. The analytes were analyzed by reversed-phase LC-MS/MS, acquiring one or two diagnostic product ions from the precursor ion for the unambiguous confirmation. The method was validated according to the European Commission Decision 2002/657/EC for the detection and confirmation of residues in products of animal origin. The limits of detection and limits of quantitation were found to be 0.2 ng/mL and 1.0 ng/mL, respectively. The accuracy and precision have been determined, with recoveries in the range of 60% to 102% and the relative standard deviation less than 15% at spiked levels of 1.0 to 10.0 ng/mL.

AGFD 85 Determination of urinary free fumonisin B1 as a biomarker of exposure to dietary fumonisins in humans by HPLC and liquid chromatography-tandem mass spectrometry Qingsong Cai1, qingsong.cai@tiehh.ttu.edu, Hongxia Guan2, guan@mail.chem.sc.edu, Li Xu3, Lili Tang1, lili.tang@tiehh.ttu.edu, and Jia-sheng Wang3, jswang@uga.edu. (1) Department of Environmental Toxicology, The Institute of Environmental and Human Health, Texas Tech University, Box 41163, Lubbock, TX, (2) Department of Chemistry and Biochemistry, University of South Carolina, Columbia, Columbia, SC, (3) Department of Environmental Health Science, University of Georgia, Athens, GA Fumonisin B1 (FB1), the major bioactive form of fumonisins (FNs), is a Group 2B carcinogen and strong tumor promoter in animal studies. Dietary FN exposure has been suggested to play an etiological role in neural tube defects, esophageal and liver cancers. Urinary free FB1, which significantly correlates with oral FN exposure in several animal models, has been proposed as a prospective biomarker of exposure to FNs. In order to quantitatively assess human dietary exposure to FNs, sensitive and reliable analytical methods for urinary free FB1 in human are urgently needed. In this study, a specific and sensitive method based on HPLC-fluorescence has been built up for the determination of urinary free FB1 in human. Major efforts were put on sample preparation to maximize recovery and minimize interference of endogenetic components in human urine. The procedure essentially involved concentration of 10 mL urine on an immunoaffinity column followed by solid-phase extraction. Urinary extracts were derivatized using o-phthaldialdehyde (OPA), and OPA derivatives were separated with a reversed-phased C18 column and detected at an excitation wavelength of 340 nm and an emission