บทความที่น่าสนใจประจำเดือน สิงหาคม 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	Antitumour effects of tetrazanbigen against human hepatocellular carcinoma QGY-7701 through inducing lipid accumulation in vitro and in vivo
Author :	Xiaohong Zheng, Wei Li, Zuoping Lan, Xiaolan Yang, Longjiang Li, Yonghua Yuan, Zhu Xia, Xunguan Chen, Xinyu Zhang and Yu Yu
Journal :	Journal of Pharmacy and Pharmacology: Article first published online: 5 AUG 2015 | DOI: 10.1111/jphp.12467
Abstract :	**Objectives** Tetrazanbigen (TNBG) is a newly synthesized compound with an isoquinoline moiety, and its antitumour effects were evaluated in in-vitro and in-vivo models. **Methods** 3-[4, 5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay was used to measure the antiproliferative activity of TNBG on cancer cell lines. Antitumour activity of TNGB in vivo was also assessed in a xenograft model of human hepatocellular carcinoma QGY-7701 cell line. Cell cycle and cell apoptosis analysis was performed. **Key findings** TNBG exhibited strong antitumour efficacy against six human cancer cell lines with IC_{50} range of 2.13–8.01 μg/ml. The IC_{50} of TNBG on normal hepatic cells was 11.25 μg/ml. Lots of lipid droplets were observed in cytoplasm of human hepatocellular carcinoma QGY-7701 cells after treatment of TNBG. S phase arrest and apoptosis induction by TNBG were also found on QGY-7701 cells. Intraperitoneal injection of TNBG (1.5 mg/kg/day) resulted in significant decreases in tumour volume and tumour weight on nude mice bearing QGY-7701 cells xenografts. Results from pathological analysis in nude mice demonstrated that

	TNBG could induce lipid accumulation specifically in cancer tissue rather than in other normal organs, tissues and blood. **Conclusions** These results suggested that TNBG might exert potent antitumour activity through inducing lipid accumulation in cancer cell.
Database :	Wiley Online Library

Title :	Implementing supported self-management for asthma: a systematic review and suggested hierarchy of evidence of implementation studies
Author :	Hilary Pinnock, Eleni Epiphaniou, Gemma Pearce, Hannah Parke, Trish Greenhalgh, Aziz Sheikh, Chris J. Griffiths and Stephanie J. C. Taylor
Journal :	BMC Medicine: Volume 13
Abstract :	**Background** Asthma self-management remains poorly implemented in clinical practice despite overwhelming evidence of improved healthcare outcomes, reflected in guideline recommendations over three decades. To inform delivery in routine care, we synthesised evidence from implementation studies of self-management support interventions. **Methods** We systematically searched eight electronic databases (1980 to 2012) and research registers, and performed snowball and manual searches for studies evaluating implementation of asthma self-management in routine practice. We included, and adapted systematic review methodology to reflect, a broad range of implementation study designs. We extracted data on study characteristics, process measures (for example, action plan ownership), asthma control (for example, patient reported control questionnaires, days off school/work, symptom-free days) and use of health services (for example, admissions, emergency department attendances, unscheduled consultations). We assessed quality using the validated Downs and Black checklist, and conducted a narrative synthesis informed by Kennedy's whole

	systems theoretical approach (considering patient, practitioner and organisational components and the interaction between these). **Results** We included 18 studies (6 randomised trials, 2 quasi-experimental studies, 8 with historical controls and 3 with retrospective comparators) from primary, secondary, community and managed care settings serving a total estimated asthma population of 800,000 people in six countries. In these studies, targeting professionals (n = 2) improved process, but had no clinically significant effect on clinical outcomes. Targeting patients (n = 6) improved some process measures, but had an inconsistent impact on clinical outcomes. Targeting the organisation (n = 3) improved process measures, but had little/no effect on clinical outcomes. Interventions that explicitly addressed patient, professional and organisational factors (n = 7) showed the most consistent improvement in both process and clinical outcomes. Authors highlighted the importance of health system commitment, skills training for professionals, patient education programmes supported by regular reviews, and on-going evaluation of implementation effectiveness. **Conclusions** Our methodology offers an exemplar of reviews synthesising the heterogeneous implementation literature. Effective interventions combined active engagement of patients, with training and motivation of professionals embedded within an organisation in which self-management is valued. Healthcare managers should consider how they can promote a culture of actively supporting self-management as a normal, expected, monitored and remunerated aspect of the provision of care.
Database :	BioMed Central

Title :	Measures of Total Energy Expenditure and Its Components Using the Doubly Labeled Water Method in Rehabilitating Burn Children
Author :	Kathy Prelack, Yong Ming Yu, Maggie Dylewski, Martha Lydon, Timothy J. Keaney, and Robert L. Sheridan

Journal :	Journal of Parenteral and Enteral Nutrition: first published on August 5, 2015 as doi:10.1177/0148607115597665
Abstract :	Background: A persistent hypermetabolic state delays anabolism and growth in burned children. However, our own clinical experience has been that resting energy expenditure (REE) is not increased during the rehabilitative phase, suggesting other contributing factors. We measured total energy expenditure (TEE) and its components in rehabilitating pediatric burn patients to identify the basis for accelerated energy metabolism in this population. Materials and Methods: Children admitted with initial burns of 20% of their total body surface area (TBSA) or greater were enrolled into this prospective, descriptive study. TEE was measured using the doubly labeled water method over a 7-day period. During that period, REE was measured on 2 days by indirect calorimetry. Activity energy expenditure (AEE) was assessed using a physical activity monitoring device for a 24-hour period. TEE and REE were compared with sex-specific, age-matched, and weight-matched norms using the Dietary Reference Intakes (DRI) standards. Results: Ten children with an average burn size of 53.7% ± 20% (range, 27%–82%) of TBSA completed this study. Their mean age and weight were 10.4 ± 5.5 years and 35.8 ± 16.4 kg, respectively. Daily TEE averaged 66 kcal/kg and was 1.08% of reference DRI. REE was 92% ± 25% of predicted basal metabolic rate, not exceeding 120% as a maximum value in any child. Conclusions: TEE and REE in rehabilitating burn children are comparable to reference standards. Increased REE was not typical in our population, but measures of AEE were commonly high.
Database :	SAGE Journals

Title :	Brazilian green propolis induced apoptosis in human lung cancer A549 cells through mitochondrial-mediated pathway
Author :	Yahima Frión-Herrera, Alexis Díaz-García, Jenny Ruiz-Fuentes, Hermis Rodríguez-Sánchez and José Maurício Sforcin
Journal :	Journal of Pharmacy and Pharmacology: Article first published online: 21 JUL 2015 | DOI: 10.1111/jphp.12449
Abstract :	Objectives

Propolis effect on the growth and apoptosis of human lung adenocarcinoma (A549 cells) was investigated as well as its mechanisms.

Methods

Cells were incubated with propolis for 72 h, and 3-(4,5- dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and lactate dehydrogenase assays were employed to assess cell viability and the inhibitory concentration (IC). Apoptosis was detected by Acridine Orange/Ethidium Bromide and 4′,6-diamidino-2-phenylindole staining after 24 and 48 h of incubation with ¼ IC50 of propolis by testing the mitochondrial membrane potential ($\Delta\Psi$m) and the expression of apoptosis-related genes (p53, Caspase-3, Bax, Bcl-2, Bcl-XL, Noxa, Puma and p21) by reverse transcription polymerase chain reaction.

Key findings

Propolis displayed antiproliferative and cytotoxic effects on A549 cells in a dose- and time-dependent manner, but it did not suppress the growth of normal Vero cells. An enhanced apoptosis was seen in A549 propolis-treated cells after 48 h compared with the control cells. Propolis decreased mitochondrial membrane potential by overexpression of pro-apoptotic genes (Bax and Noxa) and reduction of the antiapoptotic gene Bcl-XL. The expression level of other genes remained unchanged (p53, Caspse-3 and Bax), whereas p21 expression was increased. Propolis induced caspase-independent apoptosis through a p53-independent mitochondrial pathway, and cell cycle arrest by upregulation of p21.

Conclusions

Although propolis induces apoptosis mainly by p53-independent manner, it may be induced by another pathway, and new insights may arise for preventing or treating lung cancer.

Database : Wiley Online Library

Title :	Impact of statin therapy on mortality in patients with sepsis-associated acute respiratory distress syndrome (ARDS) depends on ARDS severity: a prospective observational cohort study
Author :	Ashham Mansur, Maximilian Steinau, Aron Frederik Popov, Michael Ghadimi, Tim Beissbarth, Martin Bauer1 and José Hinz
Journal :	BMC Medicine: Volume 13
Abstract :	**Background** Previous investigations have presumed a potential therapeutic effect of statin therapy in patients with acute respiratory distress syndrome (ARDS). Statins are expected to attenuate inflammation in the lungs of patients with ARDS due to their anti-inflammatory effects. Clinical investigations of the role of statin therapy have revealed contradictory results. This study aimed to investigate whether pretreatment and continuous therapy with statins in patients with sepsis-associated ARDS are associated with 28-day survival according to disease severity (mild, moderate, or severe). **Methods** Patients with sepsis-associated ARDS from the surgical intensive care were enrolled in this prospective observational investigation. ARDS was classified into three groups (mild, moderate, and severe); 28-day mortality was recorded as the primary outcome variable and organ failure was recorded as secondary outcome variable. Sequential Organ Failure Assessment scores and the requirements for organ support were evaluated throughout the observational period to assess organ failure. **Results** 404 patients with sepsis-associated ARDS were enrolled in this investigation. The distribution of the ARDS subgroups was 13 %, 59 %, and 28 % for mild, moderate, and severe disease, respectively. Statin therapy improved 28-day survival exclusively in the patients with severe ARDS compared with patients without statin therapy (88.5 % and 62.5 %, respectively; P = 0.0193). To exclude the effects of several confounders, we performed multivariate Cox regression analysis, which showed that statin therapy remained a significant covariate for mortality (hazard ratio, 5.46; 95 % CI, 1.38–21.70; P = 0.0156). Moreover, after carrying a propensity

	score-matching in the severe ARDS cohort, Kaplan-Meier survival analysis confirmed the improved 28-day survival among patients with statin therapy (P = 0.0205). Patients with severe ARDS who received statin therapy had significantly more vasopressor-free days compared with those without statin therapy (13 ± 7 and 9 ± 7, respectively; P = 0.0034), and they also required less extracorporeal membrane oxygenation (ECMO) therapy and had more ECMO-free days (18 ± 9 and 15 ± 9, respectively; P = 0.0873). Conclusions This investigation suggests a beneficial effect of continuous statin therapy in patients with severe sepsis-associated ARDS and a history of prior statin therapy. Further study is warranted to elucidate this potential effect.
Database :	BioMed Central

Title :	Retinoblastoma Protein Knockdown Favors Oxidative Metabolism and Glucose and Fatty Acid Disposal in Muscle Cells
Author :	Petar D. Petrov, Joan Ribot, Isabel C. López-Mejía, Lluís Fajas, Andreu Palou and M. Luisa Bonet
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 4 AUG 2015 | DOI: 10.1002/jcp.25121
Abstract :	Deficiency in the retinoblastoma protein (Rb) favors leanness and a healthy metabolic profile in mice largely attributed to activation of oxidative metabolism in white and brown adipose tissues. Less is known about Rb modulation of skeletal muscle metabolism. This was studied here by transiently knocking down Rb expression in differentiated C2C12 myotubes using small interfering RNAs. Compared with control cells transfected with non-targeting RNAs, myotubes silenced for Rb (by 80–90%) had increased expression of genes related to fatty acid uptake and oxidation such as Cd36 and Cpt1b (by 61% and 42%, respectively), increased Mitofusin 2 protein content (∼2.5-fold increase), increased mitochondrial to nuclear DNA ratio (by 48%), increased oxygen consumption (by 65%) and decreased intracellular lipid accumulation. Rb silenced myotubes also displayed up-regulated levels of glucose transporter type 4 expression (∼5-fold increase),

	increased basal glucose uptake, and enhanced insulin-induced Akt phosphorylation. Interestingly, exercise in mice led to increased Rb phosphorylation (inactivation) in skeletal muscle as evidenced by immunohistochemistry analysis. In conclusion, the silencing of Rb enhances mitochondrial oxidative metabolism and fatty acid and glucose disposal in skeletal myotubes, and changes in Rb status may contribute to muscle physiological adaptation to exercise.
Database :	Wiley Online Library

Title :	Population Pharmacokinetics of Vancomycin in Postoperative Neurosurgical Patients
Author :	Xingang Li, Yuanxing Wu, Shusen Sun, Shenghui Mei, Jiaqing Wang, Qiang Wang and Zhigang Zhao
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 3 AUG 2015 | DOI: 10.1002/jps.24604
Abstract :	Neurosurgical procedures may damage the blood–brain barrier to allow more vancomycin distribution into the cerebrospinal fluid (CSF) from blood after intravenous administration. However, a large intersubject variability in CSF vancomycin concentration was observed. We aimed to develop a population pharmacokinetic model to guide vancomycin dosing in patients after neurosurgical operation. Blood and CSF samples were collected and determined from postoperative neurosurgical patients after vancomycin administration. A three-compartment (central, peripheral, and CSF) model was proposed to characterize the pharmacokinetics of vancomycin. A nonlinear mixed-effects modeling approach was applied to fit the blood and CSF data simultaneously. The covariate analysis found that the CSF albumin level was strongly associated with the clearance between central and CSF compartment. Visual predictive check indicated that the proposed population pharmacokinetic model agrees well with the observed vancomycin concentrations. Individualized vancomycin dosage regimens could be developed for postoperative neurosurgical patients with different CSF albumin levels through model simulations. The CSF albumin level is a determinant of CSF vancomycin concentration.
Database :	Wiley Online Library

Title :	Taking Science Seriously in the Debate on Death and Organ Transplantation
Author :	Michael Nair-Collins
Journal :	Hastings Center Report: Article first published online -- 17 JUN 2015 DOI: 10.1002/hast.459
Abstract :	he concept of death and its relationship to organ transplantation continue to be a source of debate and confusion among academics, clinicians, and the public. Recently, an international group of scholars and clinicians, in collaboration with the World Health Organization, met in the first phase of an effort to develop international guidelines for determination of death. The goal of this first phase was to focus on the biology of death and the dying process while bracketing legal, ethical, cultural, and religious perspectives. The next phase of the project will include a broader group of stakeholders in the development of clinical practice guidelines and will use expert consensus on biomedical criteria for death from the first phase as scientific input into normative deliberation about appropriate policies and practices. Surely, science alone cannot resolve the normative and philosophical questions intertwined in debates about moral status, legal and moral rights, the ethics of killing, and personhood and the nature of the self; however, scientific input is necessary for informed moral deliberation. An objective and unbiased investigation of the biology of death is independent of, and should be undertaken prior to, an analysis of the normative questions engendered by debate about determination of death. This strategy is explicitly endorsed by the International Guidelines for Determination of Death and reflects the prevailing view of these issues in the mainstream medical literature. However, this mainstream literature, exemplified by the IGDD group's recent report, does not exhibit any of the characteristics usually associated with a scientifically rigorous investigation, such as making empirically testable and falsifiable claims, a commitment to evidence and logic over authoritative assertion, or a willingness to revise hypotheses and theories in light of new evidence. Indeed, the core claims and methodologies of the mainstream medical literature on death, both of which are represented by the IGDD report, are not merely scientifically unjustified; they are not science at all. This situation creates a problem for the integrity of science and the academy, and it unjustly obscures and

	prevents legitimate democratic and moral deliberation about issues that, at bottom, are normative, not scientific.
Database :	Wiley Online Library

Title :	Fucoidan Suppresses the Growth of Human Acute Promyelocytic Leukemia Cells In Vitro and In Vivo
Author :	Farzaneh Atashrazm, Ray M Lowenthal, Gregory M Woods, Adele F Holloway, Samuel S Karpiniec and Joanne L Dickinson
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 3 AUG 2015 | DOI: 10.1002/jcp.25119
Abstract :	Fucoidan, a natural component of seaweeds, is reported to have immunomodulatory and anti-tumor effects. The mechanisms underpinning these activities remain poorly understood. In this study, the cytotoxicity and anti-tumor activities of fucoidan were investigated in acute myeloid leukemia (AML) cells. The human AML cell lines NB4, KG1a, HL60 and K562 were treated with fucoidan and cell cycle, cell proliferation and expression of apoptotic pathways molecules were analyzed. Fucoidan suppressed the proliferation and induced apoptosis through the intrinsic and extrinsic pathways in the acute promyelocytic leukemia (APL) cell lines NB4 and HL60, but not in KG1a and K562 cells. In NB4 cells, apoptosis was caspase-dependent as it was significantly attenuated by pre-treatment with a pan-caspase inhibitor. P21/WAF1/CIP1 was significantly up-regulated leading to cell cycle arrest. Fucoidan decreased the activation of ERK1/2 and down-regulated the activation of AKT through hypo-phosphorylation of Thr(308) residue but not Ser(473). In vivo, a xenograft model using the NB4 cells was employed. Mice were fed with fucoidan and tumor growth was measured following inoculation with NB4 cells. Subsequently, splenic natural killer (NK) cell cytotoxic activity was also examined. Oral doses of fucoidan significantly delayed tumor growth in the xenograft model and increased cytolytic activity of NK cells. Taken together, these data suggest that the selective inhibitory effect of fucoidan on APL cells and its protective effect against APL development in mice warrant further investigation of fucoidan as a useful agent in treatment of certain types of leukemia.
Database :	Wiley Online Library

Title :	The Slow Molecular Mobility in Amorphous Ketoprofen and Ibuprofen
Author :	Elsa Mora, Hermínio P. Diogo, andJoaquim J. Moura Ramos
Journal :	Journal of Pharmaceutical Sciences: Article first published online -- 30 JUL 2015 DOI: 10.1002/jps.24591
Abstract :	The slow molecular dynamics in two active pharmaceutical drugs, ketoprofen and ibuprofen, have been studied by differential scanning calorimetry (DSC) and thermally stimulated depolarization currents (TSDC). This study allowed finding the main kinetic features of the fast secondary (γ) relaxation, of the Johari–Goldstein relaxation, and of the main (glass transition) relaxation, in particular their distribution of relaxation times. The fragility index of the two glass formers was determined based on data from DSC and from TSDC. The obtained results were compared with those obtained by other experimental techniques, namely, dielectric relaxation spectroscopy.
Database :	Wiley Online Library