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FATTY ACID ACCUMULATION INDUCED HAIR LOSS THROUGH DEFECTIVE MITOCHONDRIAL METABOLISM

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Abstract:

In humans, hair is an essential indicator of individual self-image, identity, ethnicity, and health. Loss of hair from any part of the body for any reason is called alopecia. There are several conditions ranging from thinning hair to complete baldness. Alopecia is of two kinds, scarring alopecia and non-scarring alopecia. The scarring alopecia is divided into three types depending on the presence of inflammatory cells like lymphocytic, neutrophilic, and mixed. Scarring alopecias are typically caused by inflammation that destroys the hair follicle leading to irreversible hair loss. While the etiology and pathogenesis of PCA remain unclear, it is currently considered as an inflammatory disorder. The treatment options for PCA are limited and are not very effective in controlling the disease progression. Previous studies stated sterol intermediates of cholesterol biosynthesis initiate inflammation. A metabolomics approach was used to identify the cutaneous metabolites which are distinct and unique for PCA. and the K14-aryl hydrocarbon receptor (K14-AhR-CA) of the mouse model. . The GC/MS and LC/MS/MS techniques were used for analyzing the wild-type littermates. While the affected, unaffected and skin biopsies of K14-AhR-CA mice were also analyzed for the metabolomics. The accumulation of fatty acid in the hair follicles was the change that occurs in the K14-AhR mouse at early stages. The scalp biopsies showed more accumulation of laurate, and the FFA tissue showed accumulation of caproate. The defective metabolism of the mitochondria in the patient sample and the alopecia model is thus confirmed. Early stages of the pathogenesis of the disease confirm the reduction in the metabolism of energy while the FFA samples, as well as the K14-AhR mice, show increased oxidized glutathione (GSSG) and Decreased glutathione (GSH) levels, which suggest mitochondrial impairment. Glutathione is a critical antioxidant that reduces cellular damage due to oxidative insult. Balanced regulation of reactive oxygen species is the crucial significance of stem cell development function and survival. The accumulation of fatty acid and the oxidative stress response were observed before the loss of stem cells and the onset of inflammation in the K14-AhR mouse model and PCA samples. Our data confirm that fatty acid accumulation evokes oxidative stress and promotes inflammation and cell death in the hair follicle.

Keywords: alopecia, hair loss, PCA, K14-AhR-CA, scalp biopsies, GSSG

Regulation of TGF- β signalling pathway by miR-21 and miR-29 in obstructive sleep apnea

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Abstract: Obstructive sleep apnea (OSA) is a respiratory condition during sleep, which is of paramount importance depicted by recurrent events of upper airway obstruction and cessation of breathing. Obesity is the prime risk factor of OSA that contributes to the onset of co-morbidities such as hypertension, cardiovascular disorders, diabetes, etc. Identification of the molecular players in OSA could help in understanding its pathophysiology. This study involves the identification of miRNAs and validation of their gene targets to investigate their role as potential biomarkers. Herein, we used miRDB and TargetScan databases to identify miR-21 and miR-29 specific targets for their recognized roles in obesity and cardiovascular disorders. The expression pattern of miR-21 and miR-29 was analyzed in OSA patient cohorts using qPCR with respect to respective controls. Molecular docking analysis using PatchDoc revealed atomic contact energy scores suggesting the miRNA-target affinities. Differential expression in miR-21 and miR-29 was observed in OSA cohorts with respect to controls. Further *in-silico* analysis identified gene targets TGFBR2 and TGFBR3 to miR-21 and miR-29 respectively revealed a difference in the docking scores of the miRNA-target complex indicating binding affinity. Validation of the expression of targets demonstrated a differential expression pattern in OSA and control cohorts. This study highlights the potential of miRNAs as probable biomarkers for OSA as well as their role in regulating the genes of the TGF- β signaling suggesting its role in OSA diagnosis and management.

Keywords: Obstructive sleep apnea, miRNA, miRDB, qPCR, molecular docking, TGF- β

ANTI-ANGIOGENIC EFFECT OF BERBERINE ON HUVECS IN-VITRO AND ZEBRAFISH IN-VIVO MODELS

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Abstract: Growth and dissemination of tumor is controlled by the onset of angiogenesis. As tumor growth and development are unfeasible without angiogenesis, a vascular targeting strategy is largely adopted to ameliorate the cancer treatment paradigm. Plant-derived natural compounds have been considered as an invaluable source of therapeutic agents for long periods. Berberine is one such bioactive compound with anti-cancer properties like anti-proliferative and anti-angiogenic activity. miRNAs being key regulators of endothelial function and angiogenesis, are also attractive targets for anti-tumor strategies in cancer therapy. In this study, *in-vitro* cell model as HUVECs and *in-vivo* animal model as zebrafish embryos have been used to investigate the anticancer and anti-angiogenic effects of berberine. The results showed that berberine inhibited the major steps involved in angiogenesis like viability, invasion, migration, and tube formation ability of HUVECs. The angiostatic effect of berberine is supposedly by suppression of the pro-angiogenic genes like VEGFR2, AKT1, and RAF. Additionally, the *in-vitro* angiostatic effect of berberine is also mediated by the up-regulation of anti-angiogenic miR-15b-5p. Furthermore, berberine inhibited the expression of inter-segmental vessel formation in zebrafish embryos by markedly suppressing the expressions of proangiogenic genes *vegfr2*, *vegfr2*, *survivin*, *angpt-1*, *angpt-2*, and *tie-2*. The study outcomes are the first of its kind to highlight the angiostatic role of berberine and provide detail about the molecular connections between tumor response and natural compounds. These experimental findings might serve as novel insights towards cancer therapy and prevention.

Keywords: angiogenesis, HUVECs, berberine, proangiogenic genes, angiostatic, cancer therapy.

THE ROLE OF miRNAs IN CANCER DEVELOPMENT

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Abstract: miRNAs are small endogenous and non-coding RNA molecules that regulate gene expression at the post-transcriptional level by degrading or inhibiting the translation of messenger RNA. It regulates around 60% of the human genes and finely modulates cellular physiology. In recent years, deregulated miRNAs have been shown to affect the hallmarks of cancer, including maintaining proliferative signaling, evading growth suppressors, resisting cell death, activating invasion and metastasis, and inducing angiogenesis. In this context, cellular pathways, especially those which control cell proliferation, differentiation, and survival, are regulated by miRNAs. In almost all cancer types, deregulation of miRNA expression has been reported. Recent evidence has elucidated that miRNAs can act as oncogenic or tumor suppressors. The upregulation of oncogenic miRNAs leads to the inhibition and degradation of tumor suppressor gene products that modulate cell growth. In contrast, tumor-suppressor miRNAs are associated with inhibiting primary transcripts of oncogenes that promote cell proliferation. Recently, an increasing number of studies have identified miRNAs as potential biomarkers for cancer diagnosis, prognosis, and therapeutic tools. Understanding miRNA-mediated regulation in cancer and the underlying molecular mechanisms on tumor pathophysiology can aid in the development of novel theragnostic strategies to combat this deadly disease.

Keywords: miRNAs, dysregulation, oncogenic, up-regulation, molecular mechanisms, theragnostic

TITANIA ENGINEERED NANOMATERIALS IN ADVANCED CLINICAL APPLICATIONS

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Abstract: Significant progress has been achieved in the field of nanotechnology over the last decade, offering the possibility of using potent tailored biocompatible nanomaterials in biological systems for theranostic applications. Nanotechnology provides a one-of-a-kind possibility to alter matter at the atomic and particle level. The particle size remains in the range of 10-100nm that helps for the free circulation and easy penetration into the tissues. Titania is the second among the most abundantly used nanomaterials and has received substantial recognition as one of the most studied metal oxides in clinical research. Titania-based nanomaterials have already led to several breakthroughs in various applications, including photocatalysis, adsorption, and lithium-ion batteries. Also, it is utilized as a vehicle in nano-drug delivery systems for the early detection of neoplastic and non-neoplastic cells, in endoprosthetic implants, as an antimicrobial agent as well as a photodynamic therapeutic agent. Titania nanomaterials are opening new perspectives in the designing of multifunctional materials for advancement in biomedical sciences.

Keywords: biocompatible nanomaterials, theranostic, Titania, metal oxides, nano-drug delivery, photodynamic.

A RETROSPECTIVE CROSS-SECTIONAL STUDY TO FIND OUT THE ROLE OF BIOCHEMICAL PARAMETERS IN ASSESSING THE SEVERITY OF SARS COV 2

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Abstract: SARS Cov 2 viruses are a group of viruses that are responsible for the present pandemic. The clinical presentation of this pandemic has been varied from simple flu-like symptoms to severe pneumonia. It is also found to affect multiple organ systems in our body. This study was conducted to find out the variations in the biochemical parameters among SARS Cov2 patients admitted to Chettinad hospital, India. The study was conducted among 258 SARS Cov2 patients admitted to the in-patient department of the hospital. Among them, 183 were males, 75 were females. The patients were divided into three groups based on their age as 20-50, 50-80, and more than 80 years. Their liver profile, renal profile, cardiac profile, ferritin levels, and LDH levels were studied. A significant difference in the levels of ferritin, LDH, serum albumin, troponin I, CK-MB, and BNP levels were found between patients admitted in ICU and ward. There was a significant difference in the levels of total protein, serum albumin, ALT, BUN, troponin I, and CK – MB values. Regression analysis showed ferritin, LDH, and serum albumin as independent markers in predicting the disease severity. This study has shown that ferritin, LDH, and serum albumin are promising biochemical markers in finding out the outcome of SARS Cov-2 infection.

Keywords: Cardiac profile, Ferritin, Liver profile, Renal profile, SARS Cov 2, biochemical markers.

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EVALUATION OF THE EFFICACY AND SAFETY OF POLYHERBAL FORMULATION TOWARDS THE MANAGEMENT OF UNCOMPLICATED RESPIRATORY INFECTION

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Abstract: Herbal medicines have existed since ancient times and are being used widely to treat various ailments, including respiratory tract infections. The active phytochemical constituents of individual plants may not be sufficient to attain the necessary therapeutic effect. A better therapeutic effect can be achieved by combining multiple herbs in correct ratios. The study was planned to evaluate the efficacy and safety of a polyherbal formulation in treating and managing uncomplicated respiratory infections. This is a randomized controlled study including 30 patients having uncomplicated respiratory infections with signs of fever, rhinitis, sore throat, myalgia, throat pain, cough, expectoration, and headache. Participants were enrolled and allocated randomly into one of the three groups- I, II, and III. Group I participants received the standard treatment (antipyretics/antihistamine/cough syrup/nasal decongestant/amoxicillin). Group II received the polyherbal formulation (*Ocimum basilicum* L., *Citrus lemon* L., *Curcuma longa* L., *Piper nigrum* L.), and Group III received standard treatment along with polyherbal formulation. All the participants were followed up for a period of one week. Monitoring of vitals, physical and systemic examinations were done. Adverse events, if any, were also noted. Investigations like CBC and throat/nasal swab for culture were taken before starting and after completion of the treatment. The polyherbal formulation has demonstrated efficacy in reducing the clinical symptoms similar to the standard treatment.

Keywords: phytochemical, polyherbal formulation, uncomplicated respiratory infections, throat/nasal swab, CBC, clinical symptoms.

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INTERPRETATION OF QUALITY CONTROL DATA OF HORMONES AND VITAMINS USING SIX SIGMA METRICS TOOL IN CLINICAL LABORATORY

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Abstract: In the health care system, it is necessary to provide high-quality and reliable test results to patients. Many clinical laboratories are using six sigma metrics as a quality management methodology in improving the outcomes. This study was done to streamline the quality control process in our clinical laboratory by analyzing the performance of hormones and vitamins using six sigma metrics. This will enable us to identify the errors in the quality control process. The analyte performance could be further improved by doing root cause analysis and appropriate application of Westgard rules. The current study was a retrospective study conducted in the Central clinical Biochemistry laboratory, Chettinad hospital, and research institute. The Quality control data of hormones and vitamins that were assayed include free T3, free T4, TSH, luteinizing hormone, follicle-stimulating hormone, prolactin, progesterone, testosterone, human chorionic gonadotrophin, folate, and vitamin B12. Both internal and external quality control material was procured from BIO-RAD. Internal quality control data of both level 1 (Normal) and level 2 (pathological) of 9 hormones and 2 vitamins under NABL scope were collected for a period of 6 months from April 2020 to September 2020. Mean, standard deviation, and coefficient of variation were calculated for each level separately. The bias percentage for each hormone was calculated from external quality control data. Clinical laboratory improvement amendment (CLIA) has given acceptable performance for each analyte in terms of total allowable error (TEa). Sigma metrics for each analyte were calculated. Quality Goal Index ratio (QGI) was calculated for those hormones with a sigma value less than 6. Testosterone level 1 (6.8), level 2 (6.5) and Folate level 1 (6.9), level 2 (6.6) showed excellent performance of sigma level more than 6. The hormones, FT3 level 1 (3.7), level 2 (4.8), HCG level 2 (3.6), TSH level 1 (4.8), level 2 (4.7) and Vitamin B12 level 1 (4.4), level 2 (4.5) showed average performance with sigma level between 3.5 and 6. The hormones, FT4 level 1 (1.7), level 2 (2), HCG level 1 (2.2), Prolactin level 1 (3), level 2 (3.3), FSH level 1 (1.9), level 2 (2.0), LH level 1 (2), level 2 (1.9) and Progesterone level 1 (3.4), level 2 (3.3) showed low performance with sigma level less than 3.5. QGI was less than 0.8 for those implicating imprecision except TSH, whose QGI was 0.8, inferring both inaccuracy and imprecision in the quality control processing. Stringent rules need not be applied for hormones with $\sigma > 6$. Moreover, control limits can be relaxed to 3S so that false rejections can be minimized. For hormones with $\sigma < 6$, internal QC rules have to be strictly applied, and the root cause analysis has to be done. To conclude, six sigma metrics is a powerful quality control tool that helps to improve the performance of the clinical laboratory and hence the efficiency of the health care system.

Keywords: Sigma metrics, QC rules, CLIA, TEa, QGI, the performance of hormones.

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A CROSS-SECTIONAL STUDY ON PSYCHOLOGICAL IMPACT OF COVID-19 AMONG THE HEALTH PROFESSIONALS IN A TERTIARY CARE HOSPITAL IN TAMILNADU.

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Abstract: During the COVID-19 pandemic, healthcare professionals were subjected to longer work shifts and were burdened with unprecedented psychological stress in managing the increased health care demand. This study aimed at estimating the prevalence of burnout, other psychopathological conditions, and its determinants among the health care professionals working in a tertiary care hospital, Tamil Nadu. This was a cross-sectional study conducted among 221 health care professionals working in a private tertiary care hospital, Tamil Nadu. The study was conducted using an online questionnaire with socio-demographic profiles, COVID-19 related working factors, Hamilton Anxiety Scale, Hamilton depression scale, and Maslach Burnout Inventory. The mean age of the study participants was 44.8 ± 11.3 . The majority of the study participants were females (68.1%). 11.2% have been infected with COVID-19 in the last 1 year. The mean MBI- emotional exhaustion score was 28.4 ± 8.7 , the mean MBI depersonalization score was 5.8 ± 3.2 , and the mean MBI- personal accomplishment was 32.9 ± 11.3 . 32.8% and 31.7% had moderate and severe levels of emotional exhaustion, 11.2 % and 13.1% had a moderate and severe level of depersonalization, and 33.2% and 31% had a moderate and severe level of reduced personal accomplishment. 21.6% and 3.1% had mild/ moderate and severe/ extreme score in HAMA and 22.6% and 1.9% had mild/ moderate and severe/ extreme score in HAMD. Effective and timely strategies towards improving mental health should be recommended.

Keywords: Hamilton Anxiety Scale, Hamilton depression scale, Maslach Burnout Inventory, emotional exhaustion score, depersonalization score, HAMA, and HAMD.

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IN-VITRO ANTI-VIRAL ACTIVITY OF FEMA SAKTHI™ AGAINST HUMAN CORONAVIRUS (HCOV) ON VERO CELLS

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Abstract: Fema Sakthi™ (FS) is a herbomineral capsule that includes extracts of *Hydrophilaspinosa*, *Mucuna pruriens*, *Orchis mascula*, *Prunus amygdalus*, sulfide of mercury (Jathilingam), coral basma (pavalaparpam) and pearl parpam (muthuparpam), which are reported to have anti-cancer, anti-viral, anti-inflammatory, and immune-modulatory properties. The present study was undertaken to evaluate the anti-viral activity of FS on African green monkey kidney cells (VERO) against the Human corona Virus. The human coronavirus (HCoV-229E) was obtained from American Type Culture Collection (ATCC; VR-740; Rockville, MD, USA) and African green monkey kidney cell (VERO E6) from NCCS (Pune, India). The TCID₅₀ (Median Tissue Culture Infectious Dose) i.e., the dilution of virus that causes a cytopathogenic effect or cell death in 50% of the wells of the Human Coronavirus was determined using the Reed-Muench method. After infecting the VERO E6 cells with 100 TCID₅₀ HCoV-229E virus, the cells were treated with 62.5, 125, 250, 500 & 1000 µg/ mL concentrations of FS extract in DMEM. The cell viability was observed under an inverted microscope with 0.1% crystal violet dye. FS at the concentration of 62.5 and 125 µg/mL showed cell growth and inhibition of cytopathic effect. The selected higher test concentrations (500 & 1000 µg/ mL) of FS showed a strong cytotoxicity effect, and therefore, it is concluded that at lower concentrations, the virucidal effect is seen while at higher concentrations, because of cell death it is not concluded to have the IC₅₀ value.

Keywords: Murine splenocytes, HCoV-229E, VERO Cells, TCID₅₀, Fema Sakthi™, DMEM.