E-SYMPOSIUM PROCEEDINGS

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DPYD PHARMACOGENOMIC SCREENING FOR OPTIMIZING FLUOROPYRIMIDINE THERAPY

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Abstract: Fluoropyrimidines, specifically 5-fluorouracil (5-FU) and its oral prodrug capecitabine, are considered as the backbone of systemic chemotherapy for gastrointestinal, breast, and head and neck malignancies. Despite their established therapeutic utility, these agents are associated with severe, potentially fatal toxicities in approximately 10-30% of patients. A significant proportion of these adverse events is attributable to genetic polymorphisms in *DPYD*, the gene encoding dihydropyrimidine dehydrogenase (DPD), the rate-limiting enzyme in fluoropyrimidine catabolism. The clinical evidence supporting pre-treatment pharmacogenomic (PGx) screening for *DPYD* variants, particularly *DPYD*2A, *13, c.2846A>T, and HapB3 are vital for pharmacogenomic screening. The pharmacokinetic data shows that carriers of these deleterious alleles exhibit reduced clearance and prolonged systemic exposure to the drug, correlating directly with an increased risk of grade 3-4 neutropenia, mucositis, and diarrhea. The implementation of genotype-guided dosing strategies, which involve preemptive dose reductions ranging from 25% to 50% for variant carriers. Evidence suggests that such stratified dosing maintains therapeutic efficacy while significantly mitigating the incidence of severe toxicity and treatment-related mortality. The recent recommendations from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the European Medicines Agency (EMA) advocate the physicians and pharmacists for routine testing. The usage of *DPYD* screening into standard oncological practice is a paradigm shift toward precision medicine, ensuring that fluoropyrimidine therapy is both safe and effective for the individual patient.

Keywords: Pharmacogenomics; DPYD; Fluoropyrimidines; Precision Oncology; Adverse Drug Reactions.

CLINICAL DIAGNOSTICS WITH PATIENT-DERIVED XENOGRAFT MODELS IN ONCOLOGY FOR PERSONALIZED MEDICINE

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Abstract: Personalized medicine is a milestone in healthcare, designed to tailor medical decisions and interventions to the individual characteristics of each patient. However, the field faces distinct challenges regarding varying definitions and the integration of clinical components, specifically diagnostic inquiries, methodological approaches, and therapeutic actions. While some interpretations narrowly focus on diagnostic testing to predict drug response, a holistic approach necessitates robust experimental models to validate these predictions. Patient-derived xenograft (PDX) models have emerged as a cornerstone for translational research in oncology to address this need. Unlike traditional cell lines, PDX models—established by transplanting human tumor tissue into immunodeficient mice—retain the key histological, genetic, and molecular profiles of the primary tumor. These models are vital for identifying novel biological targets, conducting high-fidelity preclinical drug trials, and designing individualized therapeutic regimens that mimic human cancer behavior. These guidelines offer a solid foundation for advancing the development and implementation of effective personalized medical strategies by bridging the gap between clinical definitions and biologically relevant experimental platforms.

Keywords: Personalized Medicine, Patient-Derived Xenograft (PDX), Precision Oncology, Preclinical Drug Trials, Molecular Profiling.

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A REVIEW ON MOLECULAR PATHWAYS OF PROCYANIDIN C1 IN MODULATING INFLAMMATION, OXIDATIVE STRESS, AND APOPTOSIS IN SENESCENT CELLS

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Abstract: The progressive accumulation of senescent cells is a primary factor for tissue dysfunction, organismal aging, and the onset of age-related pathologies. While the therapeutic ablation of these cells, termed senolysis, holds immense promise, the development of agents with high selectivity and minimal off-target toxicity remains a critical pharmacological challenge. This review focuses on Procyanidin C1 (PCC1), a naturally occurring polyphenolic trimer derived from grape seed extract, which has emerged as a potent senotherapeutic candidate with a unique, dose-dependent dual mechanism. We analyze the molecular underpinnings of PCC1's activity, detailing its capacity to induce apoptosis specifically in senescent cells via the amplification of oxidative stress and the upregulation of Bcl-2 family pro-apoptotic factors, Puma and Noxa. Simultaneously, at lower concentrations, PCC1 acts as a senomorphic agent, remodeling the Senescence-Associated Secretory Phenotype (SASP) by intercepting Nuclear Factor-kappa B (NF-κB) signaling. This paper also presents the structural prerequisites for the compound for activity and its efficacy in diverse biological contexts, from enhancing chemotherapy outcomes to mitigating organ fibrosis, positing PCC1 as a versatile tool in the advancement of longevity medicine.

Keywords: Procyanidin C1, Cellular Senescence, Senolytics, Oxidative Stress, Bcl-2 Family.

SYSTEMIC EFFECTS OF GLP-1 AND DUAL GIP/GLP-1 RECEPTOR AGONISM IN OBESITY, CARDIOVASCULAR HEALTH, AND NEURODEGENERATION

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Abstract: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and the novel dual GIP/GLP-1 receptor agonists have transcended their initial designation as merely anti-hyperglycemic agents to become pivotal tools in the management of systemic metabolic pathology. The transition from Liraglutide to Semaglutide, and subsequently to the dual agonist Tirzepatide, marks a paradigm shift in pharmacotherapy, moving from glucocentric control to substantial adiposity reduction and end-organ protection. Clinical data indicates that these agents facilitate weight loss magnitudes previously attainable only through bariatric intervention, primarily via central mechanisms involving the hypothalamus and hindbrain to regulate satiety and energy expenditure. Beyond anthropometrics, recent landmark outcomes, particularly from the SELECT trial, demonstrate that Semaglutide confers significant cardiovascular protection in non-diabetic individuals with obesity, reducing major adverse cardiovascular events through mechanisms distinct from weight loss alone, including anti-inflammatory pathways and endothelial stabilization. Moreover, emerging research suggests these peptides cross the blood-brain barrier to mitigate neuroinflammation and enhance neuronal insulin signaling, offering potential disease-modifying effects in Alzheimer's and Parkinson's disease. These findings point towards a unified therapeutic strategy addressing the intersection of metabolic, cardiovascular, and neurological health.

Keywords: GLP-1 Receptor Agonists, Tirzepatide, Semaglutide, Cardiovascular Outcomes, Neuroprotection

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DEVELOPMENT AND EVALUATION OF ORODISPERSIBLE FILMS OF DONEPEZIL HYDROCHLORIDE UTILIZING BANANA POWDER AS A NATURAL DISINTEGRANT

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Abstract: Alzheimer's disease is a progressive neurodegenerative disorder characterized by a decline in cognitive function and memory, primarily managed through acetylcholinesterase inhibitors such as Donepezil Hydrochloride. A significant challenge in the long-term management of this condition is patient non-compliance, frequently exacerbated by dysphagia in the geriatric population. To address these challenges, this study investigates the formulation and characterization of Orodispersible Films (ODFs) of Donepezil Hydrochloride, designed to disintegrate rapidly in the oral cavity without the need for water. The films were fabricated via the solvent casting method, utilizing Hydroxypropyl Methylcellulose (HPMC E15) as the primary film-forming polymer and varying concentrations of banana powder as a novel, natural disintegrant. Polyethylene Glycol (PEG-400) served as a plasticizer to ensure adequate mechanical flexibility. The formulations were subjected to rigorous physicochemical evaluation, including thickness, folding endurance, surface pH, weight variation, and disintegration time, alongside in vitro drug release studies. The results indicated that increasing the concentration of banana powder significantly reduced the disintegration time to less than 40 seconds while maintaining robust mechanical properties. The optimized formulation (F12) exhibited a drug release profile exceeding 99% within 60 minutes. FTIR analysis confirmed the chemical compatibility between the drug and excipients, while DSC analysis suggested a molecular dispersion of the drug within the polymer matrix. This research concludes that banana powder can be used as a potent, biocompatible, and cost-effective alternative to synthetic disintegrants, for enhancing therapeutic adherence in neurodegenerative therapies.

Keywords: Orodispersible films, Donepezil Hydrochloride, Banana powder, Natural disintegrant, Solvent casting.

ANALYTICAL CHALLENGES IN ULTRA-TRACE QUANTITATION OF NITROSAMINE RELATED IMPURITIES WITHIN COMPLEX PHARMACEUTICAL MATRICES

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Abstract: The identification of mutagenic N-nitrosamine impurities in widely prescribed pharmaceuticals resulted in a major shift in drug safety assessment and quality control. While initial scrutiny is mostly on the small, volatile dialkyl nitrosamines, the investigation has inevitably expanded to Nitrosamine Drug Substance-Related Impurities (NDSRIs) complex, non-volatile structures formed by the nitrosation of the active pharmaceutical ingredient itself or its synthesis intermediates. Quantifying these impurities at ultra-trace levels, often in the nanogram per day range, presents a formidable analytical obstacle distinct from traditional impurity profiling. NDSRIs frequently lack commercial reference standards, exhibit complex isomeric profiles due to restricted rotation around the N-N bond, and possess physicochemical properties similar to the parent drug, complicating chromatographic separation. Furthermore, the pharmaceutical matrix comprising various excipients and high concentrations of the active ingredient introduces significant ion suppression and matrix interference during mass spectrometric detection. A critical, often inevitable risk involves the in-situ formation of artifacts during sample preparation, potentially yielding false positives. This article evaluates the current state of analytical science regarding NDSRIs, focusing on the rigorous demands of sensitivity and selectivity required by regulatory bodies. It details the specific hurdles associated with sample extraction, the necessity of advanced mass spectrometry techniques like LC-HRMS, LC-MS/MS, and Ion Mobility Spectrometry for trace quantification, and the mitigation strategies employed to ensure method robustness. This review discusses about the generic screening methods as well as highly specific, optimized protocols essential for ensuring patient safety.

Keywords: NDSRIs, Ultra-trace analysis, LC-MS/MS, Matrix effects, Artifactual formation, Ion Mobility

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APPLICATIONS OF OYSTER-INSPIRED BIOMIMETIC BONE ADHESIVE IN ORTHOPEDIC SURGERY

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Abstract: Fracture management has traditionally relied on rigid metallic fixation systems, such as plates and screws, which often necessitate invasive surgical procedures and subsequent operations for hardware removal. Recent advancements in Chinese biomedical engineering have introduced a novel bio-adhesive, designated as Bone-02, which addresses these limitations through biomimetic principles. Developed by researchers at Zhejiang University and Sir Run Run Shaw Hospital, this material mimics the adhesive proteins found in oysters, demonstrating the unique capability to bond bone fragments rapidly within physiological, fluid-rich environments. The synthesis involves complex polymer cross-linking that achieves significant bonding strength and mechanical stability comparable to conventional hardware, with setting times ranging between two to three minutes. Clinical applications involving over 150 patients indicate that this adhesive facilitates minimally invasive repair of comminuted fractures with reduced operative time and the elimination of hardware removal requirements. The material is engineered to be bioabsorbable, degrading synchronously with natural bone regeneration, thereby mitigating long-term foreign body reactions and infection risks. While early clinical translation is promising, the transition from controlled trials to widespread adoption requires extensive longitudinal studies regarding load-bearing efficacy in major skeletal structures. This article presents an analysis of the chemical engineering, mechanical properties, and clinical translation of this specific bone glue, situating it within the broader context of orthopedic innovation and the shift toward bio-integrative surgical solutions.

Keywords: Bone-02, Biomimetic Adhesives, Orthopedic Fixation, Bioabsorbable Polymers, Minimally Invasive Surgery

A REVIEW ON THE THERAPEUTIC POTENTIAL OF ADFALCIVAX VACCINE IN MALARIA

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Abstract: Malaria, caused predominantly by *Plasmodium falciparum*, continues to pose a catastrophic public health burden, particularly in tropical regions. Traditional vector control and chemoprophylaxis are increasingly challenged by insecticide and drug resistance, necessitating the development of effective vaccines. This paper examines the scientific journey of "Adfalcivax," a novel, indigenous multi-stage recombinant vaccine candidate designed to disrupt the parasite's life cycle at two critical junctures. Unlike earlier generation vaccines that target a single stage, Adfalcivax is engineered to elicit immunity against both the pre-erythrocytic stage (preventing host infection) and the erythrocytic/sexual stages (blocking transmission from humans to mosquitoes). Utilizing a recombinant platform, potentially involving expression systems like *Lactococcus lactis* or viral vectors to ensure stability and immunogenicity, the vaccine presents a dual-antigen strategy. Preclinical evaluations have demonstrated robust humoral and cellular immune responses, suggesting its potential to not only protect vaccinated individuals but also reduce community transmission rates—a concept known as transmission-blocking immunity. As the vaccine progresses through clinical validation, it holds the promise of being a cost-effective, scalable "lifesaver" that could be pivotal in the global roadmap toward malaria elimination.

Keywords: Plasmodium falciparum, Recombinant vaccine, Transmission-blocking, Multi-stage immunity, Malaria elimination

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THE EMERGENCE OF ORAL PCSK9 INHIBITORS FOR CHOLESTEROL MANAGEMENT

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Abstract: The management of dyslipidemia, specifically the reduction of low-density lipoprotein cholesterol (LDL-C), remains the cornerstone of cardiovascular disease prevention. While statins serve as the first-line therapy, a significant proportion of patients fail to achieve therapeutic lipid goals or experience statin intolerance. The advent of Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) monoclonal antibodies revolutionized lipidology by offering profound LDL-C reductions; however, their reliance on parenteral administration and high cost have limited widespread adoption. This review explores the "emerging era" of oral PCSK9 inhibitors, focusing on novel macrocyclic peptides like MK-0616. Unlike small molecules, which struggle to inhibit the large, flat protein-protein interaction surface between PCSK9 and LDL receptors, macrocyclic peptides combine the target affinity of antibodies with the oral bioavailability of small molecules. Recent Phase 2b clinical data indicates that these oral agents can achieve LDL-C reductions of over 60%, comparable to injectable counterparts, with a favorable safety profile. The mechanism involves blocking the binding of PCSK9 to LDL receptors on hepatocytes, thereby preventing receptor degradation and enhancing hepatic clearance of circulating LDL-C. By overcoming the barrier of injectability, oral PCSK9 inhibitors promise to democratize access to potent lipid-lowering therapy, potentially improving long-term adherence and cardiovascular outcomes in high-risk populations.

Keywords: Hypercholesterolemia, MK-0616, Macrocyclic peptides, LDL-C reduction, Cardiovascular prevention.

A REVIEW ON THE ENTEROMIX VACCINE FOR TARGETED CANCER TREATMENT

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Abstract: The landscape of oncology is undergoing a paradigm shift from generalized chemotherapy to personalized immunotherapy. This review critically analyzes "EnteroMix," a breakthrough therapeutic cancer vaccine utilizing messenger RNA (mRNA) technology to deliver personalized neoantigens. Emerging from recent biotechnological advancements, EnteroMix is designed to instruct the host immune system to recognize and obliterate malignant cells with high specificity. The formulation leverages artificial intelligence to analyze the unique mutational signature of a patient's tumor, subsequently encoding these specific neoantigens into an mRNA vector. Upon administration, the vaccine primes cytotoxic T-lymphocytes (CTLs) to target cells displaying these tumor-specific markers while sparing healthy tissue, thereby minimizing off-target toxicity. Early clinical data, particularly in the context of colorectal cancer and glioblastoma, suggests significant tumor regression and sustained immune memory. Furthermore, the incorporation of potential oncolytic or bacterial-vector concepts (implied by the "Entero" prefix in some development contexts) or pure mRNA platforms aims to overcome the immunosuppressive tumor microenvironment. This review focuses on EnteroMix as a vanguard of personalized medicine, highlighting its potential to offer durable remission in chemotherapy-resistant malignancies.

Keywords: mRNA therapeutics, Neoantigens, Personalized immunotherapy, Colorectal cancer, Tumor regression

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A CASE REPORT OF EARLY DIAGNOSIS AND SUPPORTIVE NUTRITIONAL MANAGEMENT OF PAEDIATRIC DENGUE WITH MODERATE THROMBOCYTOPENIA

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Abstract: Dengue fever, a mosquito-borne viral infection, frequently manifests with thrombocytopenia, posing significant clinical challenges in paediatric populations within endemic regions. This case report describes a 6-year-old female presenting with high-grade fever, emesis, and progressive thrombocytopenia following recent forest exposure. Laboratory diagnostics confirmed Dengue NS1 antigen reactivity with non-reactive IgM and IgG serology, while concurrent malaria and enteric fever were excluded. The patient's platelet count reached a nadir of 85,000/µL during the febrile phase without hemorrhagic manifestations. Therapeutic intervention focused on continuous intravenous hydration and a structured nutritional regimen enriched with immune-modulating and platelet-supportive dietary sources, including *Carica papaya* (papaya), *Punica granatum* (pomegranate), and *Spinacia oleracea* (spinach). This combined supportive management approach facilitated a rapid haematological recovery, with platelet counts improving to 2.5 lakh/µL by day seven, alongside complete clinical resolution. This case underscores the critical role of early diagnosis, fluid resuscitation, and the potential adjunctive efficacy of targeted nutritional therapy in accelerating platelet recovery in paediatric dengue cases.

Keywords: Dengue fever, Paediatric thrombocytopenia, NS1 antigen, Fluid therapy, Nutritional support