INNOVATIVE DRUG SELECTION, STORAGE, AND SHELF-LIFE STRATEGIES FOR EXPLORATION SPACEFLIGHT

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Objective

Conduct a literature review to summarize the current state of knowledge regarding novel approaches to prioritization, quality optimization, and safety & efficacy validation of the exploration spaceflight drug formulary

- Targeted search criteria for publications from 2019 – 2024:
  - Pharmaceutical formulary optimization
  - Innovative drug storage / packaging
  - Pharmaceutical stability characterization and validation

Pharmaceutical Stability and Shelf Life

Problems:

- The spaceflight environment may promote drug degradation
- Drug stability testing is warranted to validate drug quality and efficacy
  - Characterizes how pharmaceuticals vary with environmental factors and time
  - Chromatographic (HPLC, UPLC) analyses require drug sample destruction, organic solvents, and a large equipment footprint, all unsuitable for spaceflight

Optimization Strategies:

Innovative Drug Quality Assessment: Statistical modeling techniques, Nondestructive pharmaceutical analysis

- Risk-Based Predictive Drug Assessment:
  - Modeling Approaches to Reimagine Stability (MARS):
    - Accelerated Stability Assessment Program (ASAP), Accelerated Stability Modeling (ASM), Risk-Based Predictive Stability (RBPS) (McMahon et al., 2020)
    - Accelerated Predictive Stability (APS) (Gonzalez et al, 2022)
- Nondestructive Drug Stability Assessment:
  - Raman spectroscopy provides non-destructive safety / quality assessments of finished pharmaceutical products (FPPs) (Silge et al., 2022)
    - Satellite laboratory "toolkit" (portable handheld Raman & Fourier Transform Infrared Spectrometers): Real-time direct analysis / identification > 650 APIs in 68 days (Lanzarotta et al., 2023)
  - Machine vision systems (MSV): Non-destructive, process analytical technology (PAT) for real-time tablet dissolution (Galata et al., 2021)
    - Meloxicam tablet dissolution (Meszaro et al., 2024)

References

Daniels, V.R., & Williams, E.S. (2023). Exploring the complexities of drug formulation selection, storage, and shelf-life for exploration spaceflight. Br J Clin Pharmacol., 1-10

Daniels, V.R., & Williams, E.S. (2024, October 8-10). Innovative Drug Selection, Storage, and Shelf-Life Strategies for Exploration Spaceflight". 13th International Association for the Advancement of Space Safety (IAASS) Conference, "Building a Safe, Secure, and Sustainable Space", Prague, Czech Republic. E-Poster ID 209

Pharmaceutical Formulary Optimization

Problems:

- Loss of medication resupply to replace exhausted or degraded medications
- Reduced / prioritized formulary necessary due to limited cargo space

Optimization Strategies:

Novel treatment modalities, medical technologies, smart medical systems:

- Physiologically based pharmacokinetic (PBPK) modeling: A computational tool for characterizing drug pharmacokinetics / toxicokinetics; enabling drug instability risk assessments (Fisher et al., 2020)
  - Machine learning (ML), and artificial intelligence (AI) can improve and advance the PBPK framework (Deepika & Kumar, 2023; Chou &Lin, 2023)
- Drug Repurposing: Selection of drug formulary candidates capable of delivering multiple medical countermeasures (MCM)
  - Biologic product Romiplostim (Nplate®), approved idiopathic thrombocytopenic purpura treatment, repurposed for hematopoietic acute radiation syndrome (Madrid & Chang, 2022)
  - Phenothiazines (e.g. PMZ) transformed into antimicrobials by laser irradiation, repurposed for multiple drug resistance during spaceflight (Simon et al., 2021)
- On-demand drug production:
  - Chemputing: Synthetizing drug molecules using a modular chemical-robot system, or "Chemputer" (Seoane-Viaño et al., 2022)
    - Doxycycline, theophylline, gentamycin (Chakka & Chede, 2023)
    - Melatonin, famotidine, acetaminophen, zolpidem tartrate (Milliken et al, 2024; Tabriz et al., 2023; Yang & Kim, 2023; Giri & Maniruzzaman, 2022; Adamov et al., 2022)
- Wearable self-contained devices with embedded sensors to detect, diagnose, monitor, and communicate health and performance data (Nkurunziza et al., 2022)
  - Rings, sleep masks, patches, smartwatches, sensing garments
  - Spacesuit exoskeleton monitoring EKG, BP, sleep cycle, body temperature (Krittanawong et al., 2023)

Pharmaceutical Packaging and Storage

Problems:

- Inadequate protection against the spaceflight environment may compromise drug stability / shelf-life

Optimization Strategies:

Innovative Drug Packaging and Storage may enhance drug stability and shelf-life

- Desiccant film technology (active-blister package): Thin (0.3 mm) extrude polymers - molecular sieve and silica gel desiccant (Mandal et al., 2022)
- Oxygen scavengers (Bazzoli et al., 2023)
- Glucose oxidase, laccase Specialized coatings (Ng et al., 2022)
- Film coating: A thin film acting as moisture-barrier around the API core (e.g. synthetic polymers, plasticizers, pigments)
- Encapsulation: Envelops the API with polymers via spray / freeze-drying / complex coacervation
- Modified atmosphere packaging (MAP): Controls package internal atmosphere (Kumar et al., 2024; Czerwinski et al., 2021)
  - Active MAP uses gas mixtures (e.g. N_2, O_2, CO_2)
  - Passive MAP uses package permeability to regulate the atmosphere
- UV-blocking composite material biopolymer films with synthesized nanomaterials (Jafarzadeh et al., 2023)
  - Carbon quantum dots: Protective carbonaceous nanomaterials (e.g. pH sensing, antioxidant, UV-shielding, photostability)
- Barriers constructed with lunar or Martian soil were proposed as viable protective pharmaceutical storage on the Moon and Mars (Chakravarti et al., 2022)