School of Pharmaceutical Sciences & Technology

Curriculum for
Fellowship Program in

Drug Discovery Approaches for Emerging and Persistent Microbial Threats

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Course Title: Drug Discovery Approaches for Emerging and Persistent Microbial Threats
Course Type: FELLOWSHIP
Duration: 360 Hours (can be structured as 24 Credits)
Mode: Lectures, Practical's /Hands-on, Project

Overview

The Fellowship in Drug Development and Antimicrobial Resistance is an advanced, specialized postgraduate program designed to address the critical global health challenge of antimicrobial resistance (AMR) while providing comprehensive training in pharmaceutical innovation and drug discovery. This fellowship integrates cutting-edge knowledge from medicinal chemistry, pharmacology, microbiology, regulatory science, and translational research to prepare professionals who can contribute meaningfully to the development of novel antimicrobial agents and alternative therapeutic strategies.

The program addresses the urgent need for new antibacterial, antifungal, antiviral, and antiparasitic agents in the context of rising multidrug-resistant (MDR) and extensively drug-resistant (XDR) pathogens. Fellows will gain expertise in the entire drug development pipeline—from target identification and lead optimization to preclinical development, clinical trials, regulatory approvals, and post-market surveillance. Special emphasis is placed on understanding resistance mechanisms, implementing One Health approaches, developing innovative therapeutic modalities (including bacteriophages, antimicrobial peptides, immunotherapeutics, and CRISPR-based interventions), and navigating the complex regulatory and economic landscape of antimicrobial drug development.

Objectives:

Upon completion of the course, the fellow shall be able to:

- Comprehend the global burden of antimicrobial resistance, including epidemiological trends, socioeconomic impact, and public health implications across healthcare, veterinary, agricultural, and environmental sectors
- Apply advanced knowledge of molecular mechanisms underlying antimicrobial resistance including horizontal gene transfer, efflux pumps, target modification, enzymatic inactivation, and biofilm formation
- Design and execute drug discovery programs for novel antimicrobial agents utilizing target-based, phenotypic, and fragment-based screening approaches
- Optimize lead compounds through medicinal chemistry principles including structure-activity relationship (SAR) analysis, pharmacokinetic/pharmacodynamic (PK/PD) optimization, and toxicity profiling
- Conduct preclinical development activities including in vitro antimicrobial susceptibility testing, time-kill kinetics, resistance selection studies, and animal efficacy models
- Navigate the regulatory pathway for antimicrobial drug development including Investigational New Drug (IND)/Clinical Trial Application (CTA) applications, clinical trial design (Phase I-III), and regulatory submissions to FDA, EMA, and Central Drugs Standard Control Organization (CDSCO)

- Evaluate alternative and adjunctive therapeutic strategies including bacteriophage therapy, antimicrobial peptides (AMPs), anti-virulence compounds, quorum sensing inhibitors, immunotherapeutics, and microbiome modulation
- Implement antimicrobial stewardship programs and infection prevention strategies to optimize antimicrobial use and minimize resistance development
- Apply computational and artificial intelligence approaches to antimicrobial drug discovery including machine learning for compound prediction, molecular docking, and resistance mechanism analysis
- Address the economic and market challenges in antimicrobial development including push/pull incentives, subscription models, and public-private partnerships
- Integrate One Health principles connecting human, animal, and environmental health in AMR surveillance, prevention, and control
- Design and conduct translational research bridging laboratory discoveries to clinical applications in antimicrobial development

Course Outcome:

CO No.	Course Outcome
CO1	Analyze the global epidemiology of antimicrobial resistance, identify priority pathogens as per WHO bacterial and fungal priority lists, and evaluate the impact of resistance on clinical outcomes, healthcare costs, and mortality rates using evidence-based data.
CO2	Design comprehensive drug discovery strategies for novel antimicrobials incorporating target identification and validation, high-throughput screening (HTS), structure-based drug design (SBDD), and lead optimization using medicinal chemistry principles and computational approaches.
CO3	Execute and interpret preclinical pharmacology studies including minimum inhibitory concentration (MIC) determination, time-kill kinetics, hollow fiber infection models (HFIM), resistance selection frequency, and in vivo efficacy models for antibacterial, antifungal, and antiviral agents.
CO4	Navigate the regulatory pathway for antimicrobial drug development from IND/CTA submission through Phase I-III clinical trials, demonstrating understanding of FDA's Qualified Infectious Disease Product (QIDP) designation, Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD), and EMA regulatory frameworks.
CO5	Evaluate and propose implementation strategies for alternative antimicrobial approaches including bacteriophage therapy, antimicrobial peptides, anti-virulence agents, immunotherapeutics, microbiome modulation, and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-based interventions, supported by current clinical evidence and pipeline analysis.

Teaching & Learning Methods:

- Interactive Lectures with Case Studies: Comprehensive theory sessions integrated with real-world examples from recent antimicrobial approvals, failed clinical trials, and resistance outbreaks
- Laboratory Training: Hands-on experience in microbiology laboratories conducting antimicrobial susceptibility testing, resistance mechanism studies, and phenotypic/genotypic characterization

- Drug Discovery Workshops: Practical sessions on computational drug design, molecular docking, virtual screening, and structure-activity relationship analysis using industry-standard software
- Regulatory Simulations: Mock IND submissions, protocol reviews, and regulatory authority interactions to prepare for real-world regulatory challenges
- Industry Expert Sessions: Guest lectures from pharmaceutical companies, regulatory agencies, biotechnology firms, and global health organizations actively working in AMR
- Journal Clubs: Critical appraisal of recent publications from Nature, Science, The Lancet, and specialized journals on antimicrobial research and resistance
- Clinical Trial Design Exercises: Developing Phase I-III protocols for antimicrobial agents considering special populations, resistance surveillance, and adaptive trial designs
- AMR Surveillance Projects: Participation in institutional or regional antimicrobial resistance monitoring programs and data analysis
- Interdisciplinary Collaborations: Working with microbiologists, infectious disease physicians, pharmacologists, and public health experts on AMR challenges
- Virtual Laboratory Tours: Online access to pharmaceutical research and development (R&D) facilities, biosafety level-3 laboratories, and Good Manufacturing Practice (GMP) manufacturing units
- Research Seminars: Regular presentations by fellows on assigned topics, research progress, and literature reviews
- Innovation Challenges: Hackathons and design challenges focused on novel solutions to AMR problems

Syllabus

Theory - 10 Credits (150 Lecture Hours)

Module I- Drug-Resilient Microbes: Global Challenge and Underlying Mechanisms (35 Lecture Hours)

- Global burden of antimicrobial resistance: epidemiology, mortality (1.27 million deaths attributable in 2019), and economic impact
- WHO Bacterial Priority Pathogens List 2024: 24 pathogens across 15 families categorized as critical, high, and medium priority
- WHO Fungal Priority Pathogens List 2022: critical, high, and medium priority fungal threats
- ESKAPE pathogens: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species
- Molecular mechanisms of resistance: β-lactamases (Extended-Spectrum Beta-Lactamases [ESBLs], carbapenemases, AmpC), target modification, efflux pumps (Resistance-Nodulation-Division [RND], ATP-Binding Cassette [ABC], Major Facilitator Superfamily [MFS] families), reduced permeability, biofilm formation
- Horizontal gene transfer: conjugation, transformation, transduction, mobile genetic elements (plasmids, transposons, integrons)
- Multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug resistant (PDR) definitions and clinical implications
- Resistance in Gram-negative bacteria: Carbapenem-Resistant Enterobacterales (CRE), Carbapenem-Resistant Acinetobacter baumannii (CRAB), MDR Pseudomonas aeruginosa

- Resistance in Gram-positive bacteria: Methicillin-Resistant Staphylococcus aureus (MRSA), Vancomycin-Resistant Enterococci (VRE), penicillin-resistant Streptococcus pneumoniae
- Mycobacterial resistance: Multidrug-Resistant Tuberculosis (MDR-TB), Extensively Drug-Resistant TB (XDR-TB), rifampicin-resistant tuberculosis
- Antifungal resistance: azole-resistant Aspergillus, Candida auris, fluconazole-resistant Candida species
- Antiviral and antiparasitic resistance patterns
- One Health approach: human, animal, agricultural, and environmental resistance interconnections
- AMR drivers: overuse/misuse in healthcare and agriculture, inadequate infection prevention, environmental contamination
- AMR surveillance systems: WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS), national networks, laboratory capacity building
- Socioeconomic impact: healthcare costs, mortality, impact on vulnerable populations in Low- and Middle-Income Countries (LMICs)

Module 2: Drug Discovery and Development Pipeline for Antimicrobials (40 Lecture Hours)

- Drug discovery overview: target-to-market stages, timelines, costs, success rates
- Target identification and validation: genomics, proteomics, metabolomics, essential gene identification
- Established antimicrobial targets: cell wall synthesis, protein synthesis, nucleic acid synthesis, metabolic pathways
- Novel targets: type II topoisomerases, FtsZ inhibitors, lipoprotein transport (Lol pathway), fatty acid biosynthesis (FabI inhibitors), peptidoglycan synthesis
- High-throughput screening (HTS): compound libraries, screening technologies, hit identification
- Fragment-based drug discovery (FBDD) and structure-based drug design (SBDD)
- Medicinal chemistry: structure-activity relationship (SAR) analysis, physicochemical properties, Lipinski's Rule of Five, metabolic stability
- Pharmacokinetic/pharmacodynamic (PK/PD) principles: time-dependent killing, concentration-dependent killing, Area Under the Curve/Minimum Inhibitory Concentration (AUC/MIC), time above MIC (T>MIC), maximum concentration/MIC (Cmax/MIC) ratios
- In vitro testing: MIC determination (broth microdilution, disk diffusion, E-test), automated systems
- Time-kill kinetics and bactericidal/fungicidal activity
- Resistance studies: mutant prevention concentration (MPC), resistance frequency, serial passage
- Combination therapy: synergy testing (checkerboard, time-kill), Fractional Inhibitory Concentration Index (FICI) calculations
- Biofilm activity assessment
- In vivo models: murine thigh infection, lung infection, peritonitis, neutropenic models
- Hollow fiber infection model (HFIM): dynamic PK/PD simulation
- Preclinical toxicology: acute, repeat-dose, genotoxicity, reproductive toxicity
- Absorption, Distribution, Metabolism, and Excretion (ADME) studies: tissue penetration (Central Nervous System [CNS], bone, lung)

- Formulation development and Good Manufacturing Practice (GMP) manufacturing

Module 3: Clinical Development and Regulatory Pathways for Antimicrobials (40 Lecture Hours)

- Regulatory landscape: FDA, EMA, Pharmaceuticals and Medical Devices Agency (PMDA), CDSCO, International Council for Harmonisation (ICH) guidelines
- Investigational New Drug (IND) application: pre-IND meetings, Chemistry, Manufacturing, and Controls (CMC), nonclinical pharmacology/toxicology, clinical protocols
- Clinical Trial Application (CTA) for EMA
- Phase I trials: first-in-human, dose escalation, safety, pharmacokinetic (PK) characterization
- Phase II trials: proof-of-concept, dose-ranging, efficacy signals, PK/PD target attainment
- Phase III trials: pivotal efficacy/safety, superiority vs. non-inferiority designs, regulatory endpoints
- Indication-specific requirements: complicated Urinary Tract Infections (cUTI), complicated Intra-Abdominal Infections (cIAI), Hospital-Acquired Bacterial Pneumonia/Ventilator-Associated Bacterial Pneumonia (HABP/VABP), bloodstream infections, Acute Bacterial Skin and Skin Structure Infections (ABSSSI)
- FDA Qualified Infectious Disease Product (QIDP) designation: eligibility, benefits (fast track, priority review, 5-year exclusivity extension)
- Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) pathway: criteria, advantages for narrow-spectrum agents
- Breakthrough Therapy and Accelerated Approval pathways
- Adaptive trial designs: platform trials, master protocols, basket trials
- Microbiological considerations: pathogen identification, endpoints, resistance surveillance
- Companion diagnostics: rapid tests, molecular diagnostics, Antimicrobial Susceptibility Testing (AST) requirements
- New Drug Application (NDA)/Biologics License Application (BLA) submissions: content, review timelines, advisory committees
- Marketing Authorization Application (MAA) for EMA: centralized, mutual recognition, decentralized procedures
- Post-approval: pharmacovigilance, Phase IV studies, Risk Evaluation and Mitigation Strategies (REMS)
- Labeling: indications, dosage, warnings, susceptibility testing information
- Regulatory challenges: enrollment difficulties, non-inferiority margins, ethical considerations
- International harmonization: relevant ICH guidelines
- Orphan drug designation and pediatric investigation plans

Module 4: Alternative Therapeutic Strategies and Responsible Drug Use (35 Lecture Hours)

- Bacteriophage therapy: biology, lytic cycles, phage-host specificity, cocktail development, clinical trials
- Engineered bacteriophages: CRISPR-enhanced phages, synthetic biology
- Endolysins and lysins: mechanisms, advantages, clinical development

- Antimicrobial peptides (AMPs): cationic peptides, defensins, cathelicidins, LL-37, membrane disruption
- Anti-virulence strategies: virulence factor targeting, toxin neutralization, adhesion inhibitors
- Quorum sensing inhibition: bacterial communication principles, small molecule inhibitors
- Immunotherapeutics: monoclonal antibodies (mAbs) (bezlotoxumab), vaccines (pneumococcal, meningococcal, typhoid)
- Microbiome modulation: Fecal Microbiota Transplantation (FMT) for Clostridioides difficile, microbiome-based therapeutics, live biotherapeutics
- Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas systems: sequence-specific killing, reversing resistance, diagnostic applications
- β-lactamase inhibitors: avibactam, vaborbactam, relebactam, diazabicyclooctanes (DBOs), boronic acids
- Efflux pump inhibitors: targeting multidrug efflux systems
- Nanotechnology: nanoparticles (silver, gold, zinc oxide), nanocarriers, biofilm penetration
- Photodynamic therapy and antimicrobial photodynamic inactivation
- Drug repurposing: screening approved drugs (auranofin, ebselen)
- Antimicrobial stewardship principles: Centers for Disease Control and Prevention (CDC) core elements, leadership, accountability, action, tracking, reporting, education
- Stewardship strategies: audit and feedback, formulary restriction, dose optimization, Intravenous (IV)-to-oral conversion, de-escalation
- Diagnostic stewardship: appropriate testing, rapid diagnostics, biomarkers (procalcitonin, C-Reactive Protein [CRP])
- Infection prevention and control: hand hygiene, environmental cleaning, contact precautions, Healthcare-Associated Infection (HAI) surveillance
- Vaccination as AMR prevention
- Global initiatives: WHO Global Action Plan on AMR, national action plans, Global Leaders Group on AMR

Practical/Hands-on Component: 8 Credits (120 Lab Hours)

1. **Microbiology and Antimicrobial Susceptibility Testing (30 hours):**
   - Bacterial culture techniques and identification
   - Minimum Inhibitory Concentration (MIC) determination by broth microdilution
   - Disk diffusion (Kirby-Bauer) method
   - E-test for MIC determination
   - Time-kill curve analysis
   - Checkerboard assay for drug synergy
   - Biofilm formation and eradication assays
   - Resistance mechanism identification: β-lactamase detection, carbapenemase assays
2. **Computational Drug Discovery and Molecular Modeling (30 hours):**
   - Molecular docking using AutoDock, Glide, or Molecular Operating Environment (MOE)
   - Virtual screening of compound libraries

- Pharmacophore modeling
- ADME prediction using Swiss ADME, QikProp
- Ligand-based drug design
- Protein structure visualization using PyMOL, Chimera
- Structure-activity relationship (SAR) analysis
- Machine learning applications in antimicrobial discovery

3. **Regulatory Affairs and Clinical Trial Documentation (30 hours):**
   - Mock IND preparation: nonclinical, CMC, clinical protocol sections
   - Phase II/III protocol development for antimicrobial trials
   - Informed consent form preparation
   - Case Report Form (CRF) design
   - Statistical analysis plan development
   - Regulatory submission dossier (Common Technical Document [CTD] format) overview
   - Reviewing FDA/EMA guidance documents
   - QIDP and LPAD pathway applications
4. **AMR Surveillance and Data Analysis (30 hours):**
   - Collection and interpretation of institutional antibiogram data
   - AMR trend analysis using WHO Network for Surveillance of Antimicrobial Resistance (WHONET), R, Python
   - Whole Genome Sequencing (WGS) data interpretation for resistance genes
   - Phylogenetic analysis of resistant strains
   - Outbreak investigation and epidemiological analysis
   - Antimicrobial consumption data analysis
   - Reporting to national and international surveillance systems
   - Development of institutional AMR reports

Project: 6 Credits (90 Self Study/Research Hours)

The project component requires fellows to conduct original research addressing a specific challenge in antimicrobial resistance or drug development. Projects may focus on:

- Novel antimicrobial compound discovery through computational screening
- Characterization of resistance mechanisms in clinical isolates
- Development and validation of rapid diagnostic methods
- Institutional AMR surveillance and intervention strategies
- Antimicrobial stewardship program implementation and outcomes
- Alternative antimicrobial therapy evaluation (phage therapy, AMPs, combinations)
- Regulatory strategy development for novel antimicrobials
- Health economics analysis of AMR impact
- One Health approach to AMR in local/regional context

The project culminates in a written dissertation and oral presentation, demonstrating the fellow's ability to design, execute, and communicate scientific research relevant to antimicrobial resistance and drug development. Fellows are expected to critically evaluate findings in context of current literature and propose future directions or practical

applications.

References:

Textbooks & Handbooks

- Antimicrobial Drug Resistance: Mechanisms of Drug Resistance – Douglas L. Mayers, Jack D. Sobel, Marc Ouellette, Keith S. Kaye
- Drug Discovery and Development – edited by Raymond Hill and Hugh Richards
- Principles and Practice of Pharmaceutical Medicine – edited by Lionel D. Edwards, Anthony J. Fletcher, Anthony W. Fox, Peter D. Stonier
- Antimicrobial Therapy and Vaccines – edited by Victor L. Yu, Richard K. Edwards, Philip S. McKnight
- Antibiotic Discovery and Development – edited by Thomas J. Dougherty, Michael J. Pucci
- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases – John E. Bennett, Raphael Dolin, Martin J. Blaser

Key Scientific Publications

- Murray CJL et al. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet, 399(10325): 629-655
- GBD 2021 Antimicrobial Resistance Collaborators (2024). Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. The Lancet, 404(10459): 1199-1226
- Sati H et al. (2025). The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. The Lancet Infectious Diseases

Regulations, Guidelines & Ethical Standards

- WHO Bacterial Priority Pathogens List, 2024
- WHO Fungal Priority Pathogens List, 2022
- WHO Global Action Plan on Antimicrobial Resistance (2015)
- WHO GLASS (Global Antimicrobial Resistance and Use Surveillance System) Reports
- FDA Guidance for Industry: Antibacterial Therapies for Patients With Unmet Medical Need
- EMA Guideline on the Evaluation of Medicinal Products Indicated for Treatment of Bacterial Infections
- Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing
- European Committee on Antimicrobial Susceptibility Testing (EUCAST) Guidelines
- ICH Guidelines (M3, Q8, Q9)
- National Action Plan on AMR India (2023-2027)
- CDC Core Elements of Hospital Antibiotic Stewardship Programs

Journals & Professional Resources

- The Lancet Infectious Diseases
- Nature Microbiology
- Antimicrobial Agents and Chemotherapy
- Journal of Antimicrobial Chemotherapy
- Clinical Infectious Diseases
- International Journal of Antimicrobial Agents