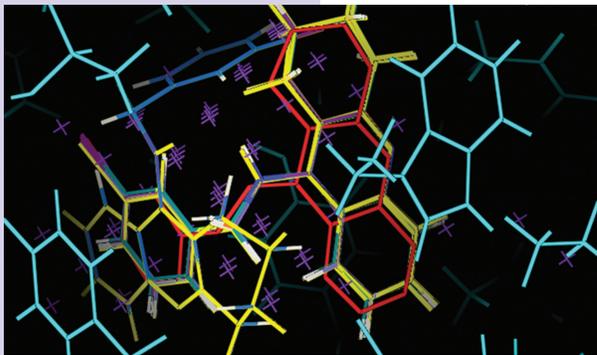


Medicinal and Process Chemistry

Integrated Services Resource



Southwest Research Institute®
San Antonio, Texas



Southwest Research Institute (SwRI®) offers integrated drug discovery, chemical development and formulation services from conception through current Good Manufacturing Practices (cGMP) clinical supply to pharma, government and academia.

Southwest Research Institute

Founded in 1947 as an independent, nonprofit research and development organization, Southwest Research Institute provides significant research, engineering, and evaluation resources for industry, business, and government. With 11 technical divisions and state-of-the-art laboratories, the Institute uses a multidisciplinary, integrated approach to solving complex problems in science and applied technology. Subject to the client's wishes, programs are kept confidential. As part of a long-held tradition, patent rights arising from sponsored research at the Institute are often assigned to the client. SwRI generally retains the rights to Institute-funded advancements.

About the cover:

The crystalized form of the drug huperzine A, a possible treatment for Alzheimer's Disease, is shown in red in this X-ray crystal structure of human acetylcholinesterase enzyme. Alternative poses of huperzine A, as determined from the Rhodium docking simulation, are in green.

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An Equal Opportunity Employer M/F/D/V
Committed to Diversity in the Workplace

Computational Drug Design Services

Institute computational chemists employ biostructure- and ligand-based drug design approaches to screen virtual compound libraries *in silico*. Applications include discovery and optimization of novel ligands for receptors, allosteric binding sites and enzyme inhibitors.

- *In silico* protein docking and simulation with proprietary Rhodium™ platform
 - Virtual library screening
 - Allosteric binding site search
- Pharmacophore model development
 - Accelrys Materials Studio®
 - Accelrys Discovery Studio®

Synthetic Services

SwRI provides custom synthesis of compounds for multiple drug discovery applications, including:

- Small molecule library synthesis
- Automated synthesis and purification
- Physicochemical characterization
- Lead development and optimization
- High potency compounds
- Peptide and protein conjugates

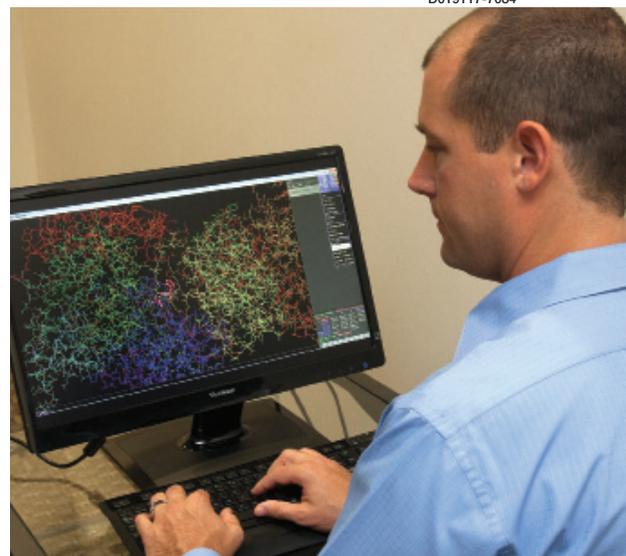
Drug Product and Specialized Drug Delivery Services

A wide variety of formulation and drug delivery platforms are available. SwRI brings decades of experience to the solution of drug delivery problems including solubility, stability, sustained drug release, tissue-selective drug release and blood-brain barrier transport.

Institute staff members have extensive experience in drug delivery solutions. For more than 20 years, SwRI chemists have aided clients with a wide range of requirements, including:

- Microencapsulation
- Customized formulations (liposomes, nanoparticles, etc.)
- Targeted drug delivery systems
- cGMP drug product manufacturing
- Project management

D019117-7084



The Institute's unique protein docking capabilities allow unbiased searches for small molecule docking sites, including allosteric sites. Rapid screening of virtual libraries is performed on multiple conformations of individual structures.

D15549-3427



Process and Analytical Development Services

To support client needs in all stages of process development and technology transfer, SwRI provides process research and kilo-scale cGMP and non-cGMP custom synthesis services for a wide range of drug development applications, including:

- Process scale-up
- Process evaluation and development
- Process optimization and critical parameter studies
- Controlled substances
- High potency drugs
- Analytical method development and validation
- Impurity and degradant isolation/synthesis
- Reference standards
- cGMP manufacturing and release testing
- ICH stability studies
- Technical writing and regulatory applications
- FDA inspected

Rhodium™ Therapeutic Drug Development Software

SwRI analysts use Rhodium to develop new ligands for protein targets and to optimize existing client-led structures. This type of simulation, called drug-protein docking, allows SwRI analysts to improve drug activity and translate these insights into improved therapeutics.

Rhodium simulations:

- Allow analysts to visualize the three-dimensional structure of a therapeutic drug in a targeted protein.
- Perform traceable, unbiased searches over the entire three-dimensional structure of the protein, whereas other software require manual pre-processing on a case-by-case basis.
- Generate alerts for specific structural features of the drug that can be improved.
- Generate feasible alternative poses for the drug that may not be revealed in the crystal structure, but could be important for biological activity.
- Provide new insights into drug binding at a protein's active site.

Rhodium generates:

- Increased throughput by screening more than 25,000 different structures per day.
- Unbiased global drug-protein docking searches
- Multiple drug conformations
- Directed structure optimization

Experienced SwRI chemists perform multi-step synthesis of target compounds using a variety of synthesis techniques and expertise. The Medicinal and Process Chemistry laboratories at SwRI can handle a diverse range of reaction scales.



Parallel synthesis and conventional synthetic methodologies are used to prepare analog libraries and perform process development and optimization. SwRI chemists commonly use automated microwave-accelerated synthesis and statistical experimental DOE approaches. Scale-up and cGMP clinical trial API synthesis services are available in our pilot plant facility.

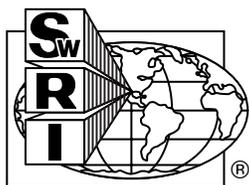


SwRI scientists have innovated the spinning disk process to yield narrow particle size distributions, and to produce micron-sized particles and a variety of process batch sizes down to a few grams with high recovery efficiency.



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We welcome your inquiries. For additional information, please contact:



***Benefiting government,
industry and the public
through innovative science
and technology***



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Quality Certification — Chemistry & Chemical Engineering Division

The Chemistry and Chemical Engineering Division of Southwest Research Institute has achieved certification to ISO 9001:2008, an internationally recognized quality standard.