Electrified Chemical Manufacturing for Secure, Onshore Production of Essential Medicines

Dr. Michael S. Emanuel · Dr. Christophe Chantre
ADIABATIC MATERIALS — SOMERVILLE, MASSACHUSETTS, USA

Adiabatic

www.adiabatic.co · info@adiabatic.co

SUMMARY

A modular, electricity-driven manufacturing platform that replaces traditional thermochemistry and metal-catalyst processes for selective, scalable production of pharmaceutical intermediates and APIs, including reactions that are hazardous, low-yielding, or impractical by conventional routes.

INTRODUCTION

The U.S. relies on fragile foreign supply chains for essential medicines:

87% of U.S. generic drug manufacturing facilities were located abroad (2021)

~80% of APIs are made overseas — India, the top U.S. supplier, imports ~70% of its own KSMs from China

~16% of APIs come directly from China — a fragile, centralized supply chain

New technologies are needed to enable safe, cost-effective domestic production.

LEARNING OBJECTIVES

- Understand how electrochemical mediator-based synthesis enables safe, clean, and more affordable domestic production of pharmaceutical intermediates and APIs critical to military and civilian healthcare.
- Highlight vulnerabilities in essential medicine supply chains and identify requirements for resilient U.S. manufacturing, including cleaner, lower-cost, and more automated production approaches.
- Explain how electrochemical systems enable modular, distributed chemical manufacturing, supporting scalable and potentially deployable production by overcoming heat and infrastructure constraints of traditional processes.

APPLICABILITY TO MEDICAL ROLES OF CARE

Enables domestic production of KSMs and APIs for military and civilian healthcare. The modular architecture supports flexible deployment and reduces reliance on global supply chains.

IMPACT TO THE WARFIGHTER / SIGNIFICANCE

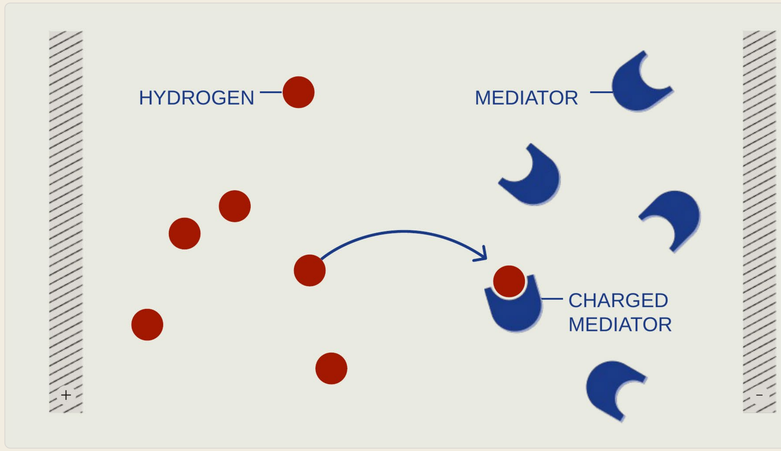
Safe, cost-effective, onshore production of essential medicines strengthens medical readiness and supply-chain resilience.

METHODS / TECHNICAL APPROACH

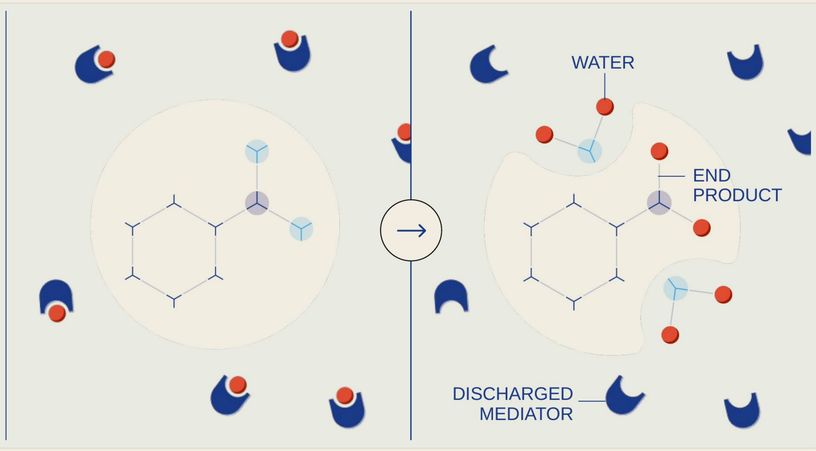
Redox mediators are first charged electrochemically in an aqueous flow system, then react with substrates in a separate biphasic reactor. At the aqueous–organic interface, mediators deliver electron–proton equivalents, enabling highly selective transformations without H_2 gas, metal catalysts, or harsh conditions.

CAPABILITY — HOW IT WORKS

Patented mediators — developed at Harvard University — separate chemical synthesis into two optimized, mild, metal-free steps.
It's clean, modular, and up to **10X cheaper** than conventional synthesis, enabling onshore production of key starting materials (KSMs) and APIs



STEP 01 · MEDIATOR CHARGING Attach hydrogen to mediators with *Electrochemical Cell*



STEP 02 · HYDROGEN TRANSFER Selectively transfer hydrogen to product with *Biphasic Reactor*

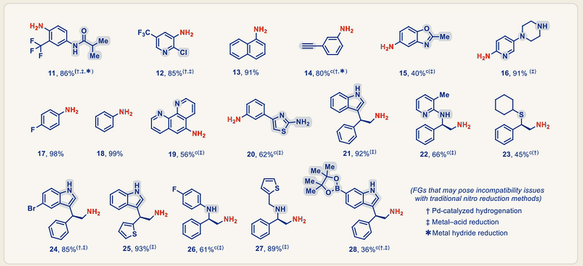
COMPETITIVE ADVANTAGE

	TRADITIONAL THERMOCHEMISTRY	ADIABATIC SYNTHESIS
Mild & Safe ambient temperature & pressure	✗	✓
No Metal Waste no metal catalysts or Pd removal	✗	✓
High Purity & Yield minimal byproducts	✗	✓
Highly Selective chemoselective reactions	✗	✓
Robust & Scalable bench to industrial, no re-optimization	✗	✓

LINEZOLID CASE STUDY

	CONVENTIONAL ROUTE	OUR ELECTRIFIED ROUTE
1. Feedstock	3-fluoro-4-morpholinonitrobenzene	Same starting material
2. Reduction	Full 6-electron reduction to aniline (Pd/C or Fe/acid)	Partial 4-electron reduction to hydroxylamine (recyclable mediator)
3. Protection	Aniline → carbamate; needs phosgene derivatives	Eliminated — hydroxylamine is already reactive
4. Ring closure	n-BuLi (pyrophoric) at −78 °C	Spontaneous at room temperature
5. Side chain	3 steps: chloride → azide → reduction	1 step: pre-functionalized epoxide
6. Final step	Acetylation	Acetylation, often in-situ

EXAMPLE COMPOUNDS PRODUCED



Thin-layer chromatography (TLC) showing selective nitro reductions to the key amine intermediates. NMR validated structures and purities above 90%.

Acetaminophen intermediate
4-aminophenol

Lidocaine intermediate
2,6-dimethylaniline

Linezolid intermediate
3-fluoro-4-morpholinoaniline

DEVELOPMENT STATUS OF THE TECHNOLOGY

The system is at TRL 5 with validated continuous operation. Scale-up to pilot production (~30 tpa) is planned over the next 2–3 years — sufficient to meet most U.S. demand for select antibiotics such as Linezolid.

RESULTS

36 molecules at bench scale

97% purity, single step

70–90% lower cost

- **Validated reaction classes** — 30+ nitro reductions[1] and H_2O_2 synthesis[2], with more in development
- **Functional-group tolerance** — aldehydes, alkenes, alkynes, aryl halides, ketones, nitriles
- **High efficiency** — >95% yield and >97% purity in a single step
- **Scalability** — modular, built from standard flow-battery stacks and mixer-settlers already proven at kiloton scale.
- **Safety** — no high temperatures or pressures, metal catalysts, or hazardous reagents
- **Economical** — low waste and byproducts, with purification steps eliminated
- **Predictable** — electrochemical conditions translate from milligram to multi-ton without re-optimization.

CONCLUSIONS

- Capable of reshoring critical pharmaceutical manufacturing — cleaner, modular, and up to 10X cheaper than traditional processes
- A new class of indirect redox chemistry — mild, metal-free, hydrogen-free: flow-battery electrochemistry coupled with biphasic hydrogen-atom transfer
- Next: validate scalable, deployable routes to U.S. Essential Medicines List drugs — Linezolid, Lidocaine, Acetaminophen

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REFERENCES 1. Alfaraidi A, Zhou J, Ni A, Su N, Xi D, Lee J, Kwan E, Aziz M, Liu R. Biphasic electrosynthesis for efficient organic reductions via hydrogen-atom transfer. ChemRxiv preprint, doi:10.26434/chemrxiv-2025-44rd7 2. Xi D, Wu Y, Li Y, Yan Z, Liu RY, Aziz MJ. Electrifying industrial hydrogen peroxide production via soft interfacial molecular mediation. Nature Chemistry 17, 1883–1890 (2025)