

FastWoRX™-M User Guide

The faster and greener way to do all your reaction work-ups and extractions

- Reduce work-up time by 50% or more
- Greener – reduce solvent use by 90% or more
- No emulsion formation
- Run parallel samples
- Works at any scale – milligrams to kilograms
- Just a simple solid separation
- Minimize solvent exposure
- Reusable
- Easy automation

FastWoRX-M is a hydrophobic and magnetic black powder that absorbs most organics. Its average particle size is about 100 mesh. Its ability to be manipulated by a magnet opens many automation possibilities. FastWoRX-M powder eliminates the need for time- and solvent-consuming liquid-liquid extraction (LLE) and allows automation of processes that now use LLE.

FastWoRX-M absorbs most hydrophobic organic compounds with a molecular weight less than 1,000 (we believe it will absorb higher molecular weight compounds but have not done testing). Hydrophilic compounds will tend to remain in the aqueous phase. FastWoRX-M has been tested with many common solvents: EtOH, MeOH, dichloromethane, dichloroethane, chloroform, ethyl acetate, diethyl ether, THF, dioxane, acetone, hexane, benzene, toluene, acetic acid, DMF and DMSO.

Below is a general procedure for using FastWoRX-M powder based on Faster Chemistry's experiences. Of course, every reaction is different and every chemist is creative so don't hesitate to try variations to get your reactions done faster than you thought possible!

Please read the SDS before use. FastWoRX-M powder should not be used with strong acids (pH < 1) or bases (pH > 14), hydrofluoric acid or fluorides.

General Procedure for Reaction Work-Up with FastWoRX-M Powder

Step 1: Conduct Your Reaction and Quench – The reaction is conducted in the usual way in an organic solvent and is quenched at completion with an appropriate aqueous solution. If quenching of the reaction is not required, FastWoRX-M powder can be added directly to the sample (go to Step 2). If your products have appreciable water solubility, a saturated solution of a suitable salt such as NaCl or NH₄Cl is recommended for quenching. Also, unlike liquid-liquid extraction, our FastWoRX-M method works well with just a small amount of quench liquid – around 5 mL of water or brine per gram of organic product usually works. If the reaction forms a solid or was done in a water miscible solvent, an appropriate water immiscible solvent should be added after quenching to dissolve the solids or form an immiscible organic phase that the FastWoRX-M powder can better absorb.

Step 2: Add FastWoRX-M Powder to the Quenched Reaction Mixture – 12 to 20 grams of FastWoRX-M powder should be added for every gram of starting materials *excluding solvents*. The absorption of more polar/water soluble compounds can be improved by quenching with a salt solution in Step 1. To minimize peak broadening during chromatography, excessive FastWoRX-M should not be used. **By its nature, FastWoRX-M is hydrophobic and it does not mix readily with an aqueous solution. Therefore, vigorous stirring or shaking should be used for good contacting. For mixtures with little or no organic solvent, wetting FastWoRX with methanol will help contacting.**

Step 3: Reduce the Solvent Volume – In Faster Chemistry’s experience, the fastest way to do a work-up while using the least amount of FastWoRX-M powder is to evaporate excess solvent at this step of the process. This can be done by rotovaping or air or inert gas sparging the quenched reaction mixture containing the FastWoRX-M powder. We recommend evaporating essentially all of solvent in this step – there should be no organic liquid visible in the mixture. As with most solids, the presence of FastWoRX-M during rotovaping may be associated with "bumping". To control bumping, we suggest using a larger flask and reasonable evaporation rates, minimizing the amount of water or brine used for quenching and avoiding sudden decreases in pressure, which will cause the now superheated liquid to boil vigorously. Sparging can be automated using equipment like Biotage’s TurboVap® or Horizon Technology’s XcelVap® automated evaporation systems.

Step 4: Separate the FastWoRX-M Powder and Wash If Needed – *Here is where your chemistry gets faster!* A unique advantage of FastWoRX-M powder is that it can easily be manipulated with a magnetic field. You can hold a strong permanent magnet at the bottom exterior of your glass reactor and simply decant the excess aqueous solution away from the retained powder with a pipette.

For many reactions, you can go directly to Step 5 after the aqueous phase is separated. If residual reactants, salts, catalysts and/or by-products are a concern with your reaction, use water or acid or base solutions to wash them from the FastWoRX-M powder held by the magnet. If using acid or base washes, you can finish with water washes to remove any residual acid or base (the approximate volume of the wash solutions in mLs is numerically equal to one-half the weight in grams of FastWoRX-M powder added in Step 2). Use the pipette decanting method described above for all these washes. If a target compound is highly water soluble, a minimal amount of a saturated inorganic salt solution (like saturated NaCl solution) should be used for the wash step – the use of salt will significantly reduce the solubility of the target during washing.

An even more powerful technique would be to use an electromagnet to capture the loaded FastWoRX-M powder from the aqueous solution by powering the electromagnet with DC. After transferring the powder to a loading cartridge or other destination, simply release it by depowering the electromagnet. Powering the electromagnet with AC of an appropriate frequency would enable “agitation” and enhanced mass transfer. These unique capabilities open many automation possibilities. Faster Chemistry is working on tools to make taking advantage of these capabilities easy.

You may also filter the FastWoRX-M powder out of the mixture. In Faster Chemistry’s experience, if you will be doing flash chromatography later, it is usually fastest and most efficient to use an appropriate dry loading cartridge as the filter. Wash using the wash solution and volume guidelines above. See the FastWoRX-S Guides for more details.

Step 5: Remove Any Solvent Remaining in the FastWoRX-M Powder as Required – Use an air or inert gas stream to evaporate any solvent remaining in the retained powder, leaving only the target compound(s) in the FastWoRX-M powder.

Step 6: Elute the Target(s) - Elute the target(s) from the FastWoRX-M powder with a suitable organic solvent. The powder can be loaded into any commercial flash chromatography system or you can elute the target(s) manually by dipping/stirring the retained powder in your desired solvent. To minimize peak broadening during chromatography, be sure the FastWoRX-M powder is uniformly distributed across the cross section of the cartridge and compressed down with a suitable tool (FastWoRX-M may have slightly broader peaks than FastWoRX-S because of differences in their supports).

Some suggestions to elute targets from FastWoRX if you're not using flash chromatography:

- Subsequent Reaction - if the yield of the first reaction is reasonable and the by-products are compatible, the FastWoRX powder loaded with organics can be directly used in the following reaction. The FastWoRX powder is then reused for the work-up of the second reaction.
- Recrystallization – extract the organics from FastWoRX powder using a hot recrystallization solvent. Two considerations: 1) you can't easily tell if most product is dissolved by the hot solvent because FastWoRX itself is a solid (this could require a separate solubility check) and 2) a small amount of the organic will remain “dissolved” in the FastWoRX powder based on the ratio of the FastWoRX **coating** volume to the sum of the recrystallization solvent volume and the FastWoRX coating volume.
- Thermally/Distillation – put the FastWoRX powder in a flask with stirring (stir bar for small scale or an agitator) and heat (up to 150 C) to drive out the organics as vapor. For larger volumes, you could use a rotovap (consider the condenser hold-up) or a distillation system with a rotary reboiler or agitation. You can add some liquid to the still pot to aid heat transfer – the liquid could be a solvent, water or brine if compatible with the process - or use a high-boiling, inert fluid like a PFPE (Krytox®) in which most compounds are insoluble.

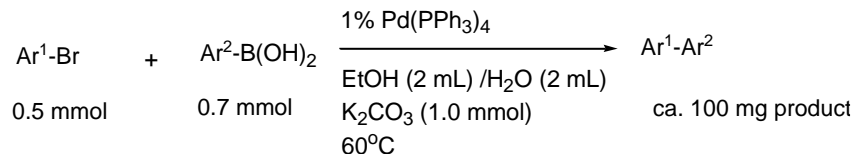
Step 7: Reuse and Disposal of FastWoRX-M – FastWoRX-M can be reused. The practicality of reuse would depend on the application. Depending on its last use, FastWoRX-M must be solvent-washed or baked-out (can be done at up to 150 C) to avoid cross-contamination.

For small scale, one-off reactions, little FastWoRX-M is used (about 2 g to absorb 100 mg of organics) and recycle is likely impractical.

We believe reuse of FastWoRX-M will be more practical for the larger-scale synthesis of a high-value compound. If you are making the same compound batch after batch in a dedicated system, there are fewer concerns about the residual compounds absorbed in the FastWoRX-M powder between batches as they are process-related. Essentially, you are recycling a “solid solvent”.

FastWoRX-M is not a hazardous waste if discarded **as supplied**. It is, of course, intended to absorb organic compounds during normal use and, therefore, used FastWoRX-M may need to be disposed of as a hazardous waste. A case-by-case determination must be made.

Using the FastWoRX work-up of this typical Suzuki reaction as an example:



1. Add water or brine (~2 mL) (to quench the reaction and dissolve the inorganic salts) and ethyl acetate (~2 mL) (added ONLY because the solvent used in this reaction is water soluble; **otherwise, no additional solvent is needed**) and FastWoRX-S (~1 gram) to the reaction mixture. Stir the mixture for ~1 min.
2. Transfer the reaction mixture from the reactor to a round bottom flask (a small amount of water or brine and ethyl acetate can be used to rinse the reactor). Then, remove the organic solvents using a rotavap (no need to separate the aqueous phase). Filter the reaction mixture using a loading cartridge. Purge the loading cartridge using vacuum for ~2 min to remove residual water and organic solvents.
3. Attach the loading cartridge to an automatic flash chromatographic system for separation.

More Information on FastWoRX™-M Powder

What is FastWoRX-M Powder?

FastWoRX-M powder is a magnetic powder support coated with a polymer. The coating is hydrophobic and absorbs most organics that have reasonably low solubility in water. The idea behind FastWoRX-M powder is quite simple. The affinity of the polymer coating for organic compounds allows those compounds to be absorbed into the polymer, similar to a sponge, while excluding water. This forms a new type of phase - a “solid solvent” phase – in which the absorbed organics are immobile compared to the usual liquid solvent. This enables easy extraction of organics from the aqueous phase by magnetic separation or simple filtration versus extraction by a liquid, as has been done for over 150 years in the well-known liquid-liquid extraction process. And, without two liquid phases, an emulsion cannot form.

FastWoRX-M powder is a fine magnetic powder (about 100 mesh) that can easily and quickly be separated - along with the absorbed organics - from the aqueous phase by a magnet or a simple filtration, enabling easy automation. Using an electromagnet allows easy collection and release of the powder. An electromagnet with a varying current allows motion for agitation and enhanced mass transfer. The target compounds can then be eluted by a suitable organic solvent.

FastWoRX-M powder is non-hazardous and reusable.

How Does Faster Extraction Compare with Other Extraction Techniques?

“Faster Extraction” (FE) – extraction done with a FastWoRX powder - and Liquid-Liquid Extraction (LLE) are quite similar in terms of their separation mechanism. Both are governed by the partition ratio — the ratio of concentrations of a compound in each phase of two immiscible phases at equilibrium. There is a wealth of partition ratio data in the literature. The main difference between FE and LLE is that separation occurs between two liquid phases in LLE and between a liquid phase and the simply separable FastWoRX-M solid phase in FE. Because FE uses only a simple solid separation, it is faster, safer and less labor intensive than LLE. Also, the FastWoRX-M solid phase prevents emulsion formation. Another advantage of FE over LLE is that it can be automated and multiple samples processed simultaneously.

The FE process is also similar to Solid Phase Extraction (SPE) in terms of handling. SPE is based on adsorption - the surface of the support is treated with various compounds to give an affinity for certain classes of target compounds in the aqueous phase. The SPE resin best suited for a given target compound is found on a case-by-case basis. In contrast, FE is based on the broad absorption of organics - the powder absorbs most organics into the bulk volume of its polymer coating. This gives FE two big advantages over SPE - near universal applicability for SPE-type applications using a single powder and capacity that is not limited by surface area. Therefore, FE can practically separate mixtures at a scale ranging from milligrams to kilograms and beyond.

What are Faster Extraction’s Advantages?

Faster Extraction combines the flexibility and scalability of LLE and the ease of handling of SPE – the best of both worlds! All the benefits of our FE technology – decreased extraction times and automation of your purification process – will reduce your cost to do extractions. Moreover, solvent use and exposure will significantly decrease, further reducing your costs and simplifying your chemistry.

Faster Extraction can be viewed as a platform technology. It is suitable for any chemical application that needs an extraction, such as chemical reaction work-up; extraction of drug metabolites from biological fluids; extraction of DNA, RNA or peptides from aqueous fluids; removal of organic pollutants from air or gases and many other extraction applications.

What Solvents Does Faster Extraction Work With?

Faster Extraction works with most of the solvents commonly used for conducting reactions and liquid-liquid extractions, such as ether, dichloromethane and ethyl acetate. Ideally, the solvent should have low water solubility. If the reaction was done in a water miscible solvent, an appropriate water immiscible solvent should be added after quenching to form an immiscible organic phase that the FastWoRX-M powder can better absorb.

What are Some Applications for FastWoRX-M Powder?

Fast chemical reaction work-up - During the discovery stage to develop pharmaceuticals, agrochemicals and other new materials, a large number of compounds need to be synthesized in amounts from milligrams to grams. For example, 10,000 compounds may be tested during drug discovery to come up with a successful drug. The bottleneck in synthesis is the work-up and purification of the reaction products rather than the actual reactions. Typically, after a reaction, a work-up procedure is needed to neutralize the active intermediate, catalyst(s), salts and polar solvents, all of which can affect chromatographic separation. The most common reaction work-up procedure is extraction using LLE, which is very time consuming. Because these syntheses deal with milligrams to grams, SPE is often not practical. FE makes work-up easy. These same considerations apply to production-scale – kilograms to tonnes - chemistry also.

DNA, RNA and protein separations - The phenol-chloroform technique is biochemistry's equivalent of LLE. It is widely used in molecular biology for isolating DNA, RNA and proteins. Nucleic acids remain in the aqueous phase and proteins separate into the organic phase or stay at the phase interface. Currently, a pipet is commonly used to manually separate the two phases, a process that is not always easy because of emulsion formation. This process is especially problematic when a large number of samples need to be processed. FE eliminates emulsion formation and would be ideal for this application.

Extraction of organic compounds from urine, blood serum, water, beverages, soil and tissue - Analysis of organic compounds in urine, blood, water, beverages, soil and tissue is crucial in clinical, food, environmental and forensic testing and other applications. The time consuming part of these analyses is usually sample preparation - many of these analyses still use traditional LLE. Numerous commercial SPE products are designed to speed-up the process. FE is an ideal method to replace time-consuming LLE and offers higher capacity and efficiency than SPE in many applications. For example, for the analysis of phenols in wastewater, EPA Method #604, "Method for Organic Chemical Analysis of Municipal and Industrial Wastewater" still calls for a time-consuming LLE with 60 mL of methylene chloride. This LLE operation is not only time intensive but also uses a relatively large amount of a toxic chlorinated solvent. FE would be ideal for this application.

Filter for the extraction of organic compounds from gases – FastWoRX-M powder can extract volatile organic compounds (VOCs) from the gas phase. Analysis of volatile organic compounds is important in air quality control, medical diagnosis and national security. FastWoRX-M powder alone or loaded with an appropriate solvent would be ideal to collect target compounds.

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