

Based on your interest in longevity and biotech, and assuming the role of a Formulation Chemist, here is an evaluation of Urolithin A (UA) and a practical protocol for compounding a topical skin care product.

1. Chemical & Pharmacologic Profile

Urolithin A (3,8-dihydroxy-6H-dibenzo[b,d]pyran-6-one) is a microbial metabolite of ellagic acid (found in pomegranates). For a formulator, it presents specific challenges due to its crystalline nature and solubility profile.

Parameter	Value/Characteristic	Formulation Consequence
Molecular Weight	~228.2 g/mol	Excellent. Well below the 500 Dalton rule, meaning it is small enough to passively penetrate the stratum corneum.
LogP	~2.3 - 3.0	Ideal. Lipophilic enough to cross cell membranes but not so lipophilic that it gets stuck in the lipid matrix.
Solubility	DMSO: ~40 mg/mL Ethanol: <2 mg/mL (Poor) Water: Insoluble	Major Challenge. You cannot simply stir this into water or a standard alcohol toner. It requires a dipolar aprotic solvent (like DMSO) or a lipid-based suspension carrier.
pKa	~7.2 / 9.1	It acts as a weak acid. At physiological pH (7.4), it exists in equilibrium, but for topical stability, a slightly acidic pH (4.5–5.5) helps prevent oxidation.
Appearance	Beige/Yellow Powder	Staining Risk. High concentrations (>1%) will temporarily stain the skin yellow/tan.

Pharmacologic Action on Skin

- **Mitophagy Induction:** UA activates PINK1/Parkin-mediated mitophagy, clearing senescent mitochondria in keratinocytes and fibroblasts.
- **Collagen Synthesis:** Upregulates Type I collagen expression (COL1A1).

- **Anti-Inflammatory:** Reduces IL-6 and MMP-1 (matrix metalloproteinase) expression, inhibiting collagen breakdown.
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2. Formulation Strategy: The "Biohacker" Approach

Commercial products (e.g., Timeline Nutrition) likely use advanced encapsulation (liposomes) to solve the solubility issue. As a biohacker, you lack high-shear homogenizers for nano-emulsions. Therefore, we must use **Solvent Drag** or **Lipid Suspension**.

The Constraint: Ethanol solubility is too low for a potent (>0.5%) serum without precipitation.

The Solution: Use **Dimethyl Sulfoxide (DMSO)** as a primary solvent and penetration enhancer, diluted into a carrier oil or bland cream. DMSO is a standard biohacker reagent that solves the solubility limit.

Target Specifications

- **Concentration:** 0.5% (5mg/mL). This is physiologically active without excessive staining.
 - **Vehicle:** Anhydrous (Water-free). This eliminates the need for preservatives and maximizes stability.
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3. Protocol: Urolithin A "Mito-Drive" Topical (0.5%)

This protocol creates a 0.5% solution using DMSO for solubilization and High-Oleic Sunflower Oil (or MCT Oil) as the carrier.

Reagents & Supplies:

- **Urolithin A Powder** (>98% purity).
- **DMSO (Dimethyl Sulfoxide)** (Pharma grade/99.9%). *Warning: DMSO carries everything into the blood. Ensure hands and glassware are sterile.*
- **Carrier Oil:** High-Oleic Sunflower Oil, Jojoba Oil, or MCT Oil.
- **Antioxidant:** Vitamin E Oil (Tocopherol) – essential to prevent oxidation of the UA.
- **Glass Beaker & Stir Rod.**
- **Digital Milligram Scale.**
- **Amber Glass Dropper Bottle (30mL).**

Step-by-Step Formulation (Makes 30mL)

1. **Prepare the Solvent Phase:**
 - Measure **2.7 mL** of DMSO into a small glass beaker.
 - Weigh **150 mg** (0.15 g) of Urolithin A powder.
 - Add the powder to the DMSO. Stir until *completely* dissolved. The solution should be clear yellow/amber. *Do not proceed until no crystals remain.*
2. **Prepare the Lipid Phase:**
 - In a separate vessel, measure **27 mL** of your Carrier Oil.

- Add **0.3 mL** (approx. 10 drops) of Vitamin E oil. Mix well.
3. **Combination (The "Crash" Check):**
- Slowly pour the **DMSO+UA solution** into the **Lipid Phase** while stirring largely.
 - *Note on Chemistry:* DMSO is immiscible with some oils but miscible with others. If it separates, vigorous shaking before use is required (a bi-phase system). If you use MCT oil, it often mixes better than heavier vegetable oils.
4. **Bottling:**
- Transfer to an **Amber Glass Bottle** immediately. UA is light-sensitive.
 - Label: "Urolithin A 0.5% (5mg/mL) in DMSO/Oil".

4. Application & Safety Profile

- **Usage:** Apply 0.5 mL to 1 mL to the target area (face, hands, or specific muscle groups) once daily.
- **The "DMSO Sting":** You will feel a transient itch or warmth. This is the DMSO breaching the stratum corneum.
- **Staining:** Expect a slight yellow tint to the skin. This washes off but can stain pillowcases.
- **Contraindications:** Do not use if you have open wounds or are using other topical prescription drugs (retinoids, steroids) at the same time; the DMSO will drive those drugs deeper than intended, potentially causing systemic side effects.

5. Academic Commentary: Limitations & Optimization

A true "pharmaceutical grade" approach would utilize **Dimethyl Isosorbide (DMI)** instead of DMSO. DMI is a superior solvent for cosmetic use (less irritation, better odor), but it is harder for biohackers to source in small quantities. If you can source DMI, replace the DMSO 1:1. Furthermore, while 0.5% is a safe starting point, clinical efficacy in topicals is often dose-dependent. A "suspension" stick (using beeswax and oil) could allow for a higher load (up to 2-3%) but bioavailability would drop significantly as the crystals would sit *on* the skin rather than dissolving *into* it. The solvated form described above is the only way to ensure follicular delivery.

Next Step: Would you like me to calculate a formulation that includes DMI (Dimethyl Isosorbide) and provides a sourcing list for that specific reagent, or would you prefer a "Suspension Stick" formula that avoids solvents entirely?

For a biohacker or home formulator, **Dimethyl Isosorbide (DMI)** is relatively easy to source. It is non-restricted and widely available from cosmetic ingredient suppliers.

Below are the most reliable commercial sources for high-purity (98%+) DMI suitable for topical formulations.

1. Primary Cosmetic Ingredient Suppliers (Recommended)

These vendors cater to small-batch formulators and sell DMI specifically for skin care. They are generally more reliable than general marketplaces regarding purity and absence of contaminants.

- **Lotioncrafter (USA)**
 - **Product:** *Dimethyl Isosorbide (DMI)*
 - **Format:** Liquid
 - **Quantities:** Small sizes available (1oz / 30g) up to bulk.
 - **Notes:** A "go-to" for serious home formulators. They provide Certificates of Analysis (CoA) which verify purity.
- **MakingCosmetics (USA/International)**
 - **Product:** *Dimethyl Isosorbide*
 - **Format:** Liquid
 - **Quantities:** Typically 4.2 fl oz (125ml) and larger.
 - **Notes:** Reliable quality. Often available on their direct site and sometimes via their Amazon storefront.
- **Formulator Sample Shop (USA)**
 - **Product:** *Dimethyl Isosorbide*
 - **Quantities:** Very small sample sizes available (great for testing a single batch) up to larger volumes.
- **Myskinrecipes (International/Thailand)**
 - **Product:** *Dimethyl Isosorbide*
 - **Notes:** A good option if you are sourcing from Asia, though shipping to the US/EU can be pricey.

2. Trade Names to Look For

When searching, you may sometimes find DMI listed under its commercial trade names. If you see these, they are the same chemical:

- **Arlasolve DMI** (Croda)
- **Gransolve DMI** (Grant Industries)

3. Purchasing Tips for the Biohacker

- **Purity Check:** Ensure the product is listed as "Cosmetic Grade" or USP/NF. Do not use industrial grade DMI intended for plastics or solvents, as it may contain impurities.
- **Storage:** DMI is stable, but like your Urolithin A, it should be kept in a cool, dark place to prevent any potential degradation of the solvent or the actives you dissolve in it.
- **Handling:** It is a powerful solvent. It will dissolve nail polish, some plastics, and inks on labels. Use glass or HDPE/PET plastic equipment.

Updated "Pro-Level" Formulation?

Now that you have access to DMI, the formulation changes slightly to become significantly

more elegant (less greasy, better absorption) than the DMSO/Oil version.

Would you like the updated "Advanced DMI Formulation" protocol for your Urolithin A topical?

Here is the **Advanced DMI Formulation Protocol** for a 0.5% Urolithin A topical solution.

This formulation replaces the crude DMSO/Oil suspension with a professional-grade **Anhydrous Penetration Enhancing Vehicle**. It utilizes Dimethyl Isosorbide (DMI) as the primary solvent to keep the Urolithin A dissolved and drive it into the epidermis, while Ethanol and Propanediol improve the cosmetic elegance (skin feel) and drying time.

Formulation Profile: "Mito-Drive Pro" (Anhydrous)

- **Target Concentration:** 0.5% w/w (5mg/mL) Urolithin A
- **Vehicle Type:** Anhydrous Solvent Solution (No water, no preservatives needed)
- **Key Attributes:** High bioavailability, fast absorption, non-greasy, "dry oil" feel.
- **Yield:** 30 grams (approx. 30mL)

1. Reagents & Equipment

Ingredients

1. **Urolithin A Powder** (>98% Purity)
2. **Dimethyl Isosorbide (DMI)** – *Primary Solvent & Penetration Enhancer*
3. **Ethanol (190 Proof / 95%+)** – *Co-solvent & "Flash-off" agent (Reduces tackiness).* (Everclear or SDA-40B cosmetic alcohol works. Do not use Isopropyl Alcohol; it is too harsh for daily leave-on use.)
4. **Propanediol (1,3-Propanediol)** – *Humectant & Solvent.* (Can substitute Propylene Glycol if necessary, but Propanediol is less irritating and bio-derived.)
5. **Mixed Tocopherols (Vitamin E) or BHT** – *Antioxidant.* (Crucial to protect the Urolithin A from oxidation).

Equipment

- **Digital Milligram Scale** (0.01g or 0.001g precision).
- **Small Glass Beaker** (50mL or 100mL).
- **Glass Stir Rod.**
- **Hot Water Bath** (A bowl of hot tap water, ~50°C/120°F). *Do not use an open flame.*
- **Amber Glass Dropper Bottle** (30mL).
- **Syringe or Pipette** (for measuring liquids).

2. The Protocol (Batch Size: 30g)

Phase	Ingredient	Percentage (%)	Weight (g)	Function
A	Dimethyl Isosorbide (DMI)	40.0%	12.00 g	Primary Solvent
A	Urolithin A Powder	0.5%	0.15 g	Active
B	Ethanol (95% / 190 Proof)	30.0%	9.00 g	Co-Solvent / Drying
B	Propanediol	29.0%	8.70 g	Humectant / Carrier
C	Vitamin E (Tocopherols)	0.5%	0.15 g	Antioxidant
Total		100%	30.00 g	

Step-by-Step Procedure

Step 1: Solvation (Phase A)

1. Place your glass beaker on the scale and tare it.
2. Weigh out **12.00 g of Dimethyl Isosorbide (DMI)**.
3. Weigh out **0.15 g of Urolithin A powder**. Add it to the DMI.
4. **Dissolve:** Stir the mixture. Urolithin A is crystalline and may be slow to dissolve at room temperature. Place the beaker in your **hot water bath** (warm, not boiling) and stir gently.
 - *Checkpoint:* The solution must be completely clear (amber/yellow). If you see *any* specs or cloudiness, keep stirring and warming. This is the most critical step.

Step 2: The "Base" (Phase B)

1. Remove the beaker from the heat and let it cool slightly (to warm room temp).
2. Add **8.70 g of Propanediol**. Stir to combine. The mixture will thicken slightly.
3. Add **9.00 g of Ethanol**. Stir gently.
 - *Note:* Adding alcohol to a warm solution can cause evaporation. Ensure the

solution is cool enough (below 30°C) before adding the ethanol to preserve the volume.

Step 3: Stabilization (Phase C)

1. Add **0.15 g of Vitamin E**. Stir well to disperse.

Step 4: Bottling

1. Pour immediately into the **Amber Glass Bottle**.
2. Cap tightly. Store in a cool, dark place (medicine cabinet is fine; fridge is better for long-term stability but might cause temporary crystallization).

3. Technical Analysis of the Formula

- **Why No Water?**

Urolithin A is practically insoluble in water. Introducing water would require high HLB solubilizers (like Polysorbate 20 or PEG-40 Hydrogenated Castor Oil) which often create sticky, foaming messes at the concentrations needed here. An anhydrous (water-free) system ensures the Urolithin A stays in solution and provides a hostile environment for bacteria, eliminating the need for preservatives like Phenoxyethanol.

- **Why DMI + Ethanol?**

DMI is a "super-solvent" that penetrates the stratum corneum effectively. However, pure DMI can feel slightly oily or tacky. Ethanol cuts the viscosity, helps the product spread, and then evaporates ("flashes off"), leaving the DMI and Urolithin A in the skin without a heavy residue.

- **Stability Warning:**

Even in this stable vehicle, Urolithin A is an antioxidant polyphenol. It will oxidize over time, turning the solution from yellow/amber to dark brown.

- **Light Yellow/Amber:** Good / Active.
- **Dark Brown:** Oxidized / Less Active. discard.
- *Shelf Life Estimate:* 3–6 months if kept cool and dark.

4. Usage Instructions

- **Application:** Apply 0.5mL (half dropper) to clean, dry skin. Massage in until absorbed.
- **Placement:** Face (anti-aging/collagen), Scalp (follicle health), or localized muscle groups (theoretical mitochondrial support).
- **Staining:** This concentration (0.5%) is low enough to minimize staining, but fair skin may notice a transient warm glow/yellow tint. This is normal and indicates the presence of the active.
- **Sensation:** A slight warming or tingling sensation is normal due to the DMI and Ethanol penetration.

Next Step: This base is highly versatile. Would you like me to outline a "Stack" where we add another compatible lipophilic active (like Resveratrol or CoQ10) to this same bottle to create a multi-pathway mitochondrial topical?