

# Study on the Application Potential of Deuterium-Depleted Water Across the Skin Barrier [1]

**Authors:** Cheng Jianwei; Li Yongyong

**Affiliation:** Institute for Biomedical Engineering & Nano Science, Tongji University School of Medicine, Shanghai 200092, China

## Abstract <sup>[1]</sup>

In recent years, the cosmetics industry has sought new strategies that allow active ingredients to penetrate the skin more effectively. Deuterium-depleted water (DDW) may serve as an efficient trans-dermal agent. This study evaluates the solubility and permeability of DDW and explores its potential as a novel strategy to enhance trans-dermal delivery in cosmetics.

**Keywords:** cosmetics; deuterium-depleted water; trans-dermal absorption

## The application potential of deuterium-depleted water in transcending the skin barrier

**Authors:** Cheng Jianwei; Li Yongyong

**Affiliation:** Institute for Biomedical Engineering & Nano Science, Tongji University School of Medicine, Shanghai 200092, China

**ABSTRACT:** In recent years, with the continuous advancement of technology and the increasing focus on health and beauty, the cosmetics industry has been facing new challenges and opportunities. One of them is how to better penetrate the effective components of cosmetics into the skin to maximize their effectiveness. Deuterium-depleted water may be an effective transdermal agent and has now attracted widespread attention. This study examines the solubility, permeability of deuterium-depleted water, and its potential application as a new transdermal strategy in cosmetics.

**KEY WORDS:** cosmetics; deuterium-depleted water; transdermal absorption

In modern society, as people's demand for health and beauty continues to grow, cosmetics, as an important tool for beauty and skin care, have become an indispensable daily necessity in people's lives. However, despite the emergence of various new products and technologies in the cosmetics field, there is still a problem that has not been fully solved, that is, how to make the active ingredients in cosmetics better penetrate the skin to exert their maximum effect [1-3]. This challenge mainly comes from the existence of the stratum corneum on the surface of the skin, which acts as a natural barrier to prevent external substances from penetrating, resulting in the active ingredients in cosmetics often not being fully absorbed by the skin [4]. In recent years, with the continuous advancement of science and technology, people have conducted in-depth research on the mechanism of cosmetics penetrating into the skin and tried to find new transdermal solutions. In this process, deuterium-depleted water has attracted widespread attention in the cosmetics field. The deuterium content in the ordinary water we drink daily is about 0.015%, deuterium-depleted water refers to water with a deuterium content of less than 0.015% [5-7]. 17O-NMR spectroscopy analysis confirmed that the molecular clusters of deuterium-depleted water are more than 50% smaller than those of ordinary water, so it is speculated that deuterium-depleted water will be easier to penetrate the skin barrier and enter the skin than ordinary water. In other words, deuterium-depleted water may be a more effective transdermal agent, which provides a new potential solution for improving the permeability of cosmetics.

As a new type of transdermal agent, deuterium-depleted water has many unique properties. First, the solubility of deuterium-depleted water is better than that of ordinary water, especially in dissolving organic components. Secondly, the molecular clusters of deuterium-depleted water are smaller than those of ordinary water, and its transdermal ability is higher. It can more

effectively promote the penetration of various ingredients through the skin barrier and improve the transdermal absorption rate of each ingredient. Therefore, using deuterium-depleted water as a solvent in cosmetics not only has good biocompatibility, but also can improve the transdermal efficiency of various ingredients in cosmetics, which brings new possibilities for the research and development and application of cosmetics. This study examined the solubility and transdermal ability of deuterium-depleted water, and analyzed its application potential as a new transdermal strategy for cosmetics.

## **1 Materials and Methods <sup>[1]</sup>**

### **1.1 Experimental Animals and Reagents**

- BALB/c female mice (6–8 weeks, SPF)
- DDW with 0.004% and 0.007% deuterium (Henan Wuji Bioengineering)
- Agarose, fluorescein isothiocyanate (FITC), rhodamine B (Sigma-Aldrich)

### **1.2 Solubility Test**

Take 3 sterile centrifuge tubes, add 1 mL of water with different deuterium contents [0.004%, 0.007% and 0.015% (i.e., ordinary water)] respectively with a pipette, then add 1 mg of FITC and 1 mg of rhodamine B powder accurately weighed with an analytical balance to the 3 waters with different deuterium contents, and then place them in an ultrasonic oscillator for oscillation and dissolution at a frequency of 150 kHz. 10 minutes after the dissolution operation is completed, observe and take pictures of the solute dissolution and the light transmittance changes of the solution with a camera.

### **1.3 Trans-dermal Ability Tests**

#### **1.3.1 In-vitro experiment**

Take 3 sterile centrifuge tubes, add 10 mL of ordinary water with a pipette, then accurately weigh 0.02 g of agarose with an analytical balance, heat in a microwave oven to dissolve, prepare 0.5% agarose solution, and add it dropwise to the sterile centrifuge tube. After standing for 2 hours, it will form a gel to simulate the skin epithelial cell membrane. Then, use water with different deuterium contents (0.004%, 0.007% and 0.015%) to prepare 1 mg/mL trypan blue solution, take 1 mL of each and drop it on top of different agarose gels, let it stand for 6 hours to simulate the process of passive drug diffusion, and observe the time and depth of transparent agarose gel penetrated by trypan blue dye.

### 1.3.2 Mouse Experiments

First, 1 mL of water with different deuterium contents (0.004%, 0.007% and 0.015%) was used to prepare 1 mg/mL rhodamine B dye solution, and 0.2 mL of dimethyl sulfoxide and 0.8 mL of water with different deuterium contents were used to determine the degree of transdermal absorption; the fluorescence area of the skin section was detected to area of the mouse, and 1 mL of FITC solution or 1 mL of rhodamine B solution was dripped on the gauze. After 4 to 6 hours, the mouse skin under the gauze was taken for tissue sectioning, and the tissue staining was photographed by confocal microscopy. The fluorescence intensity of the skin section was detected to deuterium contents were used to prepare 1 mg/mL FITC solution. Then, gauze was applied to the shaved back to determine the depth of transdermal absorption.

## 2 Results

### 2.1 Dissolving capacity of deuterium-depleted water

FITC is slightly soluble in ordinary water, with a solubility of < 0.1 mg/mL. FITC that exceeds the solubility limit will form flocculent precipitation. Therefore, the solubility of water with different

deuterium contents can be judged according to the clarity of the FITC solution. The results of this study showed that the low-deuterium aqueous solution with a deuterium content of 0.004% was the clearest, while floccules existed in ordinary aqueous solutions (Figure 1). Since fat-soluble substances such as astaxanthin are difficult to penetrate directly into the skin, if low-deuterium water with a deuterium content of 0.004% with better solubility is used, the solubility of fat-soluble active ingredients in cosmetics and the efficiency of penetrating the stratum corneum can be improved.

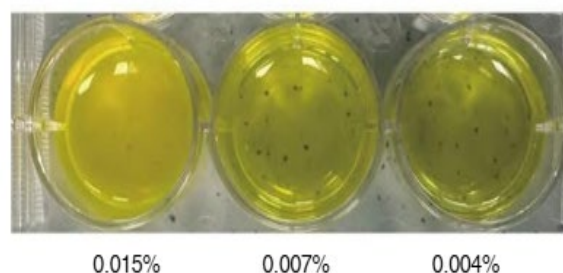
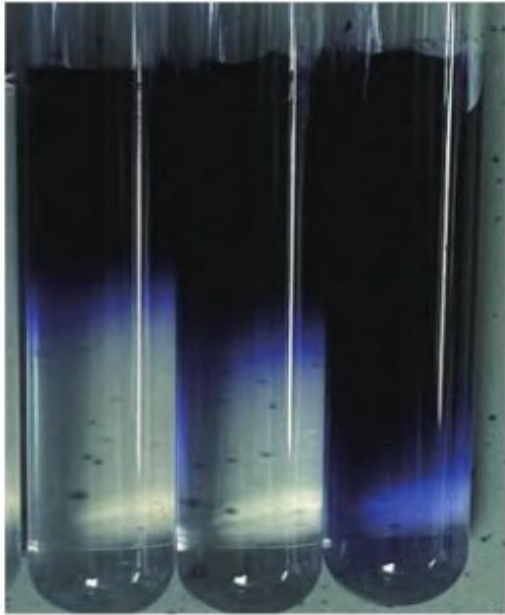


Figure 1 Solubility of FITC in water with different deuterium contents

### 2.2 Transdermal ability of deuterium-depleted water

In an in vitro experiment to investigate the transdermal ability of deuterium-depleted water, transparent agarose gel was used to simulate the skin epithelial cell membrane, and then trypan blue solution was added to simulate the passive diffusion of the drug. The results showed that the trypan blue solution prepared with deuterium-depleted water containing 0.004% deuterium penetrated the deepest into the agarose gel (Figure 2).

## Deuterium content

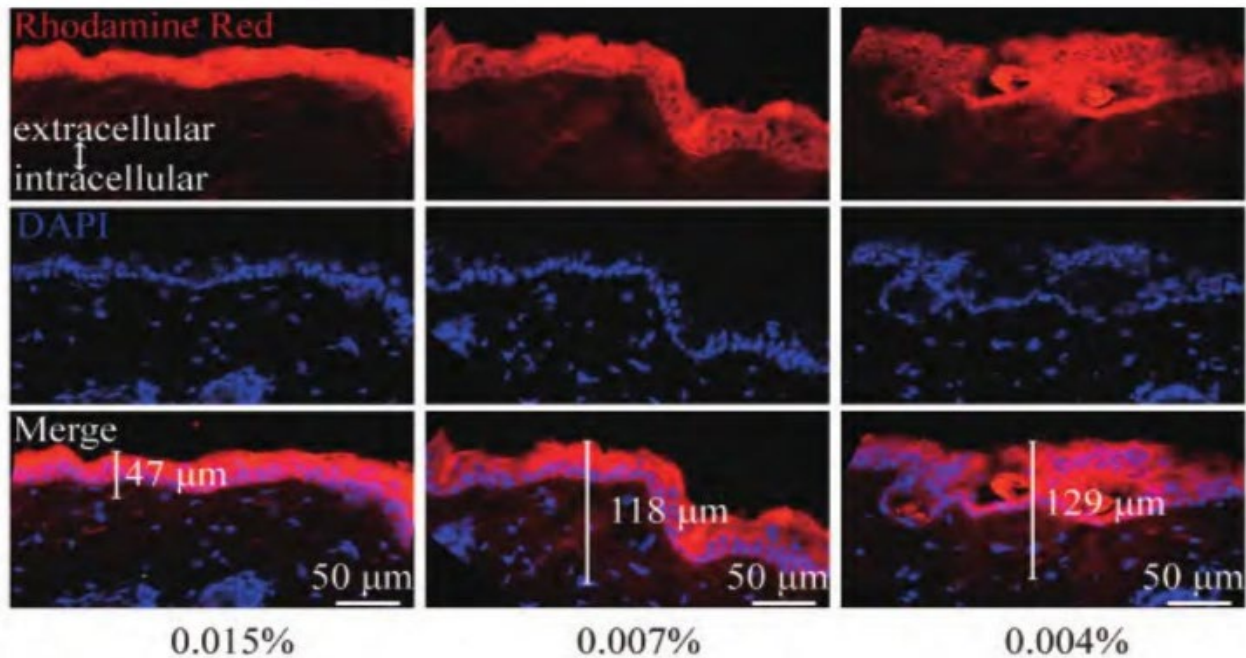


0.015% 0.007% 0.004%

Figure 2. Penetration of trypan blue solution prepared with water containing different deuterium contents into agarose gel

The results of the mouse experiment to investigate the transdermal ability of deuterium-depleted water showed that compared with ordinary aqueous solutions, the fluorescence of rhodamine B (water-soluble) solution and FITC (slightly water-soluble) solution prepared by deuterium-depleted water with a deuterium content of 0.004% penetrated into the mouse skin.

The light intensity is stronger and the penetration depth is deeper (Figures 3 and 4), indicating that using deuterium-depleted water as a cosmetic solvent can improve the penetration of active ingredients in cosmetics.



0.015%

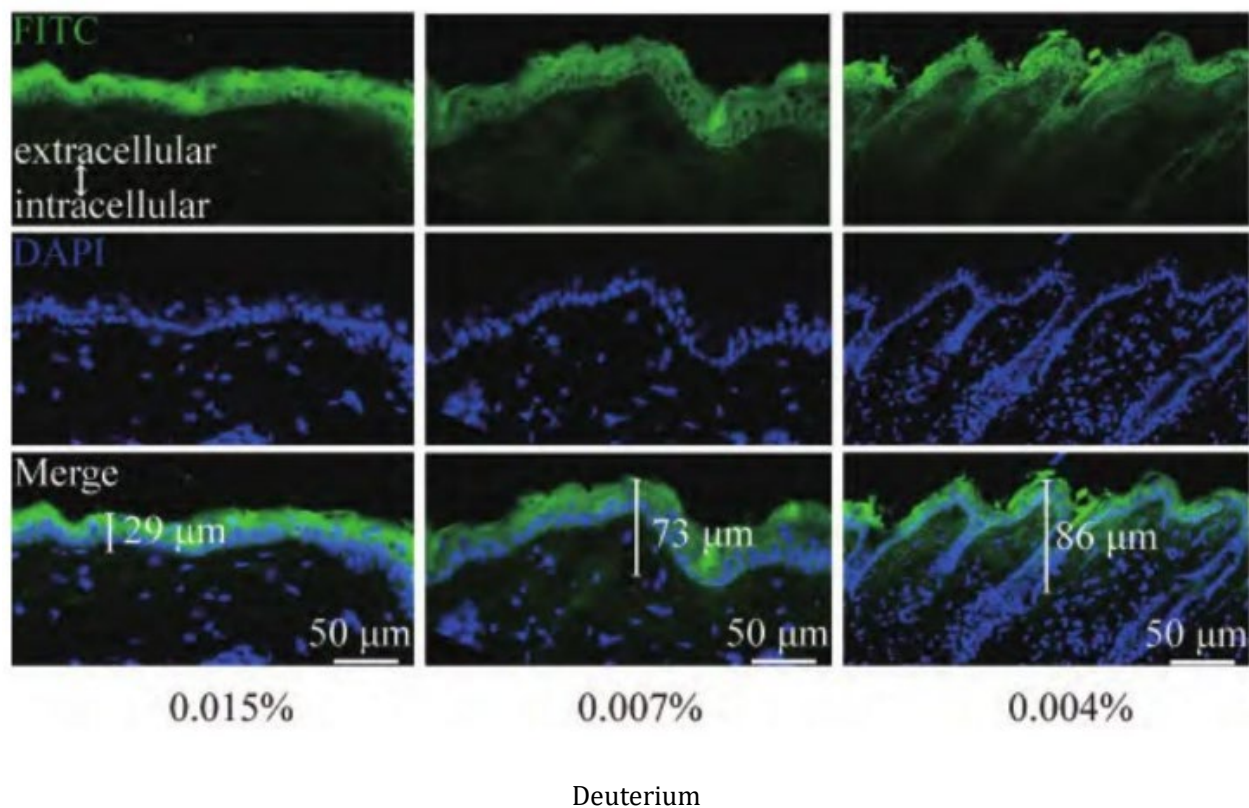
0.007%

0.004%

## Deuterium content

Upper image: Mouse skin tissue labeled with rhodamine B; Middle image: Mouse skin labeled with fluorescent dye DAPI Tissue; bottom: Mouse skin tissue co-labeled with rhodamine B and DAPI

Figure 3 Immunohistochemical examination of the penetration of Rhodamine B solutions prepared with water containing different deuterium contents into mouse skin



Upper Image: mouse skin tissue labeled with FITC; Middle: mouse skin tissue labeled with fluorescent dye DAPI; Lower: mouse skin tissue co-labeled with FITC and DAPI Figure 4 Immunohistochemical examination of tissue sections on the permeability of FITC solutions prepared with water containing different deuterium contents into mouse skin

### 3 Discussions

In order to explore the application potential of deuterium-depleted water in the field of cosmetics, this study experimentally examined the solubility and transdermal ability of deuterium-depleted water. The results showed that deuterium-depleted water has better solubility and higher transdermal ability than ordinary water and can effectively promote the penetration of various ingredients through the skin barrier. The lower the deuterium content, the more significant the effect.

Deuterium-depleted water can more easily penetrate the skin barrier than ordinary water, which may have a positive impact on the application effect of cosmetics. The ability of active ingredients in cosmetics to penetrate the skin barrier is affected by many factors, one of which is the properties of the solvent, including solubility, viscosity and surface tension. Studies have shown that the viscosity and surface tension of water play a major role in the dissolution of living substances and drugs.

The lower the viscosity and the greater the surface tension of water, the more likely it is to penetrate the skin barrier. Large water also has a detoxifying effect: due to its small molecular clusters, this water not only carries nutrients into cells, but also removes waste and toxins. Excrete cells, promote cell metabolism, and maintain cell health [8]. Due to the low viscosity and high surface tension of low-deuterium water, its solubility and transdermal ability are better than ordinary water, which makes it have great application potential in the field of cosmetics. Especially in improving the transdermal ability of cosmetics, by using deuterium-depleted water as a solvent, cosmetics can more effectively deliver active ingredients deep into the skin to moisturize, nourish and anti-aging. Delivers active ingredients deep into the skin to moisturize, nourish and anti-aging. And other skin care effects.

### References

- [1] Prausnitz MR, Langer R. Transdermal drug delivery [J]. *Nat Biotechnol*, 2008, 26(11): 1261-1268.
- [2] Qu F, Geng R, Liu Y, et al. Advanced nanocarrier- and Expert consensus report.  $\beta$ -lactam antibiotics/ $\beta$ -lactam Expert consensus on the clinical application of enzyme inhibitor combination preparations (2020 edition)[J]. *Chinese Journal of Medicine*, 2020, 100(10): 738-747.
- [3] Phatale V, Vaiphei KK, Jha S, et al. Overcoming skin barriers through advanced transdermal drug delivery approaches [J]. *JControl Release*, 2022, 351: 361-380.
- [4] Pham QD, Björklund S, Engblom J, et al. Chemical penetration enhancers in stratum corneum— relation between molecular effects and barrier function [J]. *JControl Release*, 2016, 232: 175-187.
- [5] Krasnopolsky VA, Mumma MJ, Gladstone GR. Detection of atomic deuterium in the upper atmosphere of Mars [J]. *Science*, 1998, 280(5369): 1576-1580.
- [6] Sen A, Balamurugan V, Rajak KK, et al. Role of heavy water in biological sciences with an emphasis on thermostabilization of vaccines [J]. *Expert Rev Vaccines*, 2009, 8(11): 1587-1602.
- [7] Somlyai G, Jancsó G, Jákli G, et al. Naturally occurring deuterium is essential for the normal growth rate of cells [J]. *FEBS Lett*, 1993, 317(1/2): 1-4.
- [8] Goncharuk VV, Kavitskaya AA, Romanyukina IY, et al. Revealing water's secrets: deuterium depleted water [J]. *Chem Cent J*, 2013, 7(1): 103.
- [9] Duane TM, Huston JM, Collom M, et al. Surgical Infection Society 2020 updated guidelines on the management of complicated skin and soft tissue infections[J]. *Surg Infect (Larchmt)*, 2021, 22(4): 383-399.
- [10] Castro D, Dresser L, Granton J, et al. Pharmacokinetic alterations associated with critical illness[J]. *Clin Pharmacokinet*, 2023, 2(2): 209-220.
- [11] Meta-analysis of efficacy and safety

comparison of Liuluzhu[J]. Chinese Pharmacy, 2020, 31(22): 2774-2780., Wu Zhigui

[12] Wenzler E, Gottfried MH, Loutit JS, et al. Meropenem-RPX7009 concentrations in plasma, epithelial lining fluid, and alveolar macrophages of healthy adult subjects[J]. Antimicrob Agents Chemother, 2015, 59(12): 7232-7239. [13] Chinese Medical Education Association Infectious Diseases Committee.

Expert consensus on the clinical application of mechanical/pharmacodynamic theory[J]. Chinese Journal of Tuberculosis and Respiratory Diseases

Journal of Clinical Oncology, 2018, 41(6): 409-446. [14] Clinical application of  $\beta$ -lactam antibiotics/ $\beta$ -lactamase inhibitor combination preparations