

# Study of Diffusion through the Skin of Coated L-Ascorbic Acid by Fluid Bed Technology

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## Abstract

Coating protects substances such as L-ascorbic acid from natural processes like oxidation. In this study, L-ascorbic acid was coated by fluid bed technology. A pH-dependent polymer was used as a coating material in order to release L-ascorbic acid (dissolution above pH 5.5) under conditions closest to the skin's natural condition. Different techniques were used to determine the coating (SEM and size distribution) and to evaluate the percentage of coated L-ascorbic acid and its diffusion through the skin.

## Keywords

pH Dependent Polymer, L-Acid Ascorbic, Diffusion, Fluid Bed

## 1. Introduction

Vitamin C (Vit. C) is one of the naturally occurring antioxidants in nature. Most plants and animals are able to synthesise Vit. C *in vivo* from glucose [1].

L-ascorbic acid (LAA) is the chemically active form of Vit. C. In nature, Vit. C is found in equal parts as LAA and D-ascorbic acid. These are essentially isomeric molecules and are mutually interchangeable. However, only LAA is biologically active and thus useful in medical practice. The absorption of Vit. C in the gut is limited by an active transport mechanism and hence a finite amount of the drug is absorbed despite high oral dosage. Furthermore, bioavailability of Vit. C in the skin is inadequate when it is administered orally. The use of topical ascorbic acid is therefore favored in the practice of dermatology [1].

Ascorbic acid is used as an ingredient of anti-aging cosmetic products. As an antioxidant, it protects the skin by neutralizing reactive oxygen species (ROS) generated on exposure to sunlight. In biological systems, it reduces both oxygen- and nitrogen-based free radicals and thus delays the aging process [2].

The use of ascorbic acid in cosmetic and pharmaceutical products is however

limited due to its low stability [3]. Ascorbic acid is a very unstable vitamin and is easily oxidized in aqueous solutions and cosmetic formulations.

To solve this problem of stability different strategies are being studied and the microencapsulation is a suitable technology.

Microencapsulation technology provides a strategy for enhancing retention of sensitive and expensive active components, including LAA through protection from adverse conditions and allowing delivery to the target site at the required time. Microcapsules have the potential to be very widely used in cosmetic industry applications and some of these are microencapsulation can protect sensitive core compounds from the environmental factors, including oxygen, water and light; undesirable interactions with other ingredients; other roles are to control diffusion or to isolate or control the release of an encapsulated active compounds at the right place and the right time [4].

There are a number of commercially approved shell materials available to produce various microencapsulated Not all shell materials meet all the properties needed, so they are often used in combination with other coating materials with other modifiers such as oxygen scavengers, antioxidants, chelating agents and surfactants [5].

Some microencapsulated materials are made for controlled release of the microencapsulant, perhaps during processing, storage or during final preparation prior to consumption. Commonly used methods for controlled release include temperature and moisture release for hydrophilic encapsulants. Other release methods include pH control, addition of surfactants, enzymatic release, ultrasonics, grinding, and photo-release [5].

There are numerous methods for microencapsulation of active compounds but no single encapsulation process is adaptable to all core materials or product applications. The encapsulation of ascorbic acid has been studied using different encapsulation methods: spray drying [6] [7], liposomes [8], inclusion [9], emulsification [10], etc.

In this work Fluidised Bed Coating method has been selected. This process is also known as air suspension coating. It is accomplished by suspending solid particles of the core material in an upward moving stream of air, which can be heated or cooled [5] [11].

A thin layer of coating is deposited onto the core material and full coverage is achieved by multiple passes through the air stream. Optimum encapsulation results are obtained with core particle sizes of between 50 and 500 microns.

The two most important processing variables in this process are volume of fluidized air used, which controls the height of the substrate particles in the air stream and determines their surface coating time. The other variable is air temperature. This is a critical factor as improper temperature control will result in incomplete coverage by the coating material and thus lead to a poor quality product [12]. This method is common for use in the nutritional supplement market to supply encapsulated versions of vitamins [13].

The purpose of this current study has been focused upon the influence of

coating parameters on the properties of encapsulated ascorbic acid. Morphology, particle size distribution, ascorbic acid content and diffusion were evaluated.

## 2. Materials and Methods

### 2.1. Materials

A copolymer derived from esters of acrylic and methacrylic acid that allows pH-dependent release of the active ingredient, EUDRAGIT L30 D-55 (supplied by Evonik, Germany), was used as shell material.

The core material was L-ascorbic acid (supplied by Sigma Aldrich, Spain).

### 2.2. Methods

Coating was realized in a fluid bed reactor (Uniglatt, Germany). Coating polymer was sprayed at the bottom of the reactor with help of peristaltic pump.

Particles were introduced in the reactor. Air ventilator was run. Spray was started when temperature was stabilized in the reactor (generally 25°C). After end of spraying, reactor was let stand running to finalize particle drying. Then particles were collected and analyzed.

The fixed variables were: in-process air flow 22.0 m<sup>3</sup>/h, speed of coating material intake 8 rpm, intake air pressure for spraying 1 Bar.

## 3. Characterization Tests

### 3.1. Determination of Microcapsules Morphology, Scanning Electron Microscopy (SEM)

For surface observation, a PHENON scanning electron microscope (FEI company, United States) was used. Each sample studied, LLA uncoated and particles coating, was fixed on a standard sample holder and sputter coated with gold. Samples were then examined with suitable acceleration voltage and magnification. Different samples were analyzed in order to select the most representative.

### 3.2. Particle-Size Distribution (Mastersizer)

Mastersizer E 3000 (Malvern Instruments Ltd, UK) is a particle-size analyst. It measures the particle-size distribution due to the measurement of dispersed light intensity. This fact occurs when a laser goes through the dispersed sample of particles. A unit of dispersion for dry samples was used.

### 3.3. Determination of LAA in the Microcapsules by Chromatography

LAA was determined using a Waters chromatograph, fitted with a Waters automatic injector 717 plus, Waters 600 pump and Waters 996 diode detectors, and data was handled using *Empower*. A Symmetry C18 (3.9 × 150 mm, 5 µm) column was used and as a mobile phase a mix of methanol: dihydrogen sodium phosphate 0.05 M, with pH adjusted to 2.5 with phosphoric acid 0.05 M. The proportions used were 35 methanol: 65 phosphate, expressed as a volume at a

flow rate of 0.8 ml/min. injection volume was 20  $\mu$ l and detection wavelength was 244 nm.

The corresponding LAA calibration curve was prepared using as a standard a solution of 500  $\mu$ g/ml in methanol as a standard and performing dilutions in mobile phase, to obtain a primary standard from 0.195 to 50  $\mu$ g/ml: all samples and solutions were stored away from light at all times.

### 3.4. Trans-Membrane Diffusion Trial

A test was designed to evaluate LAA diffusion from microcapsules using Franz-type vertical diffusion cells to simulate the skin, with a cellulose-acetate membrane of 0.45  $\mu$ m and 25 mm diameter, separating the donor compartment from the receptor compartment. The sample of 10 mg of microcapsules dispersed in a buffer solution of phosphate pH 7.4 was placed in the donor compartment. The receptor compartment was filled with a phosphate pH 7.4 buffer solution (approx. 6 mL) and a small mixing wand was inserted. The receptor compartments were maintained at 37°C. 1 mL samples were removed at pre-established intervals from the receptor compartment, and the same volume of phosphate pH 7.4 buffer solution was introduced to replace the lost volume. The trial was run with two microcapsule samples for 24 hours, and the accumulated quantity of ascorbic acid in the receptor medium was quantified using the HPLC method described in Paragraph 3.3.

## 4. Results and Discussion

### 4.1. Scanning Electron Microscopy (SEM)

The morphology of the coating was studied by scanning electron microscopy (SEM). **Figure 1(a)** shows the micrograph of LAA uncoated and **Figure 1(b)** shows the micrograph of LAA coated by fluid bed.

Comparing SEM images of the coated and uncoated particles, it can be seen that coating layer was deposited on the particles homogeneously. They are rounder and the edges of the particles have disappeared: post-coating morphology is completely different.

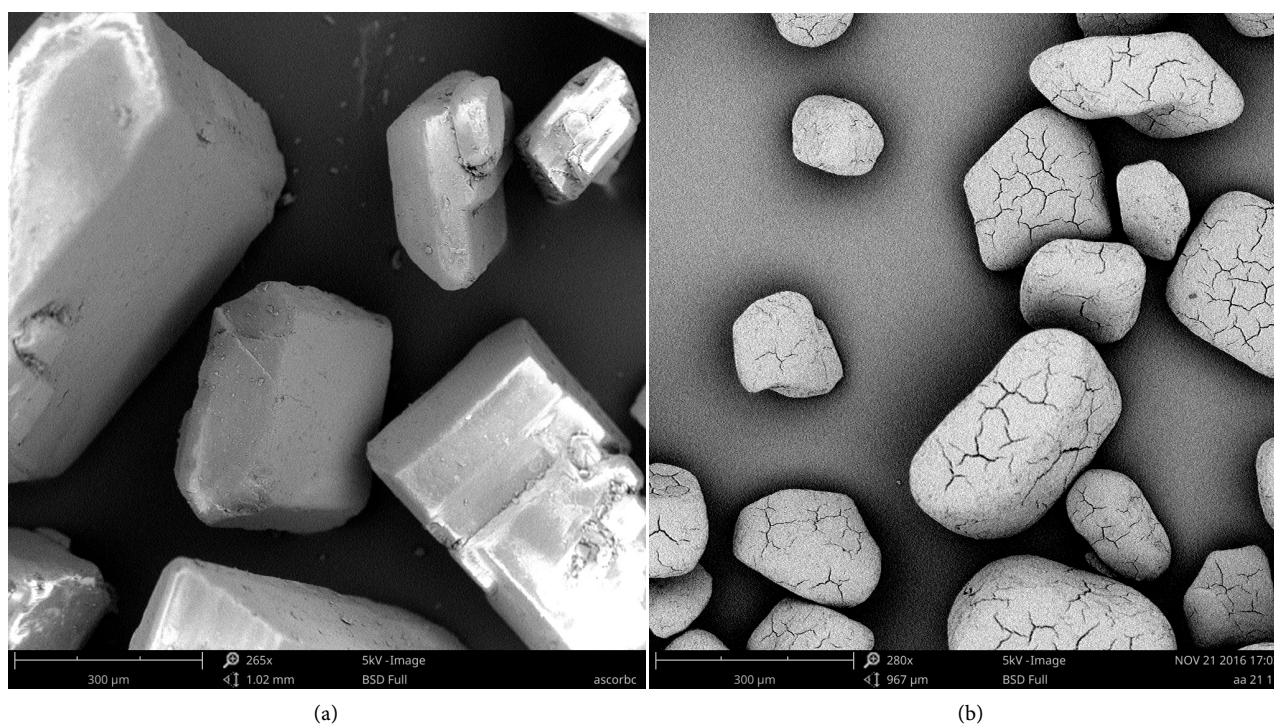
### 4.2. Particle-Size Distribution (Mastersizer)

The SEM images analyzed previously demonstrated the appearance of a coating, and although the size was determined as variable and it could have been estimated, the particle size test offers objective and more precise measurements. **Figure 2** compare the size distribution for LLA uncoated and coated, in order to affirm that exist the coating.

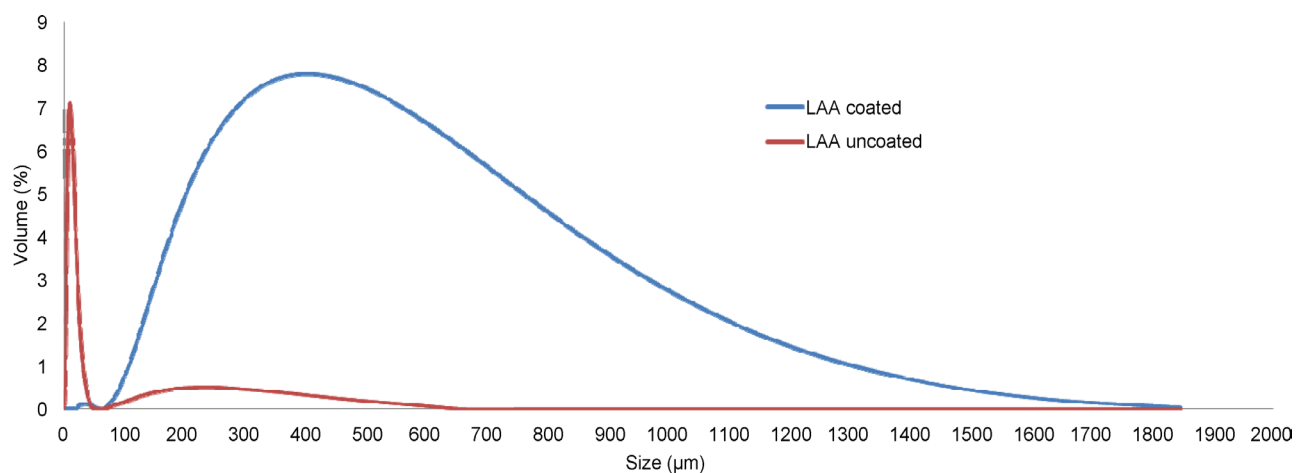
As can be seen in **Figure 2**, microparticle size is greater in coated particles, confirming the existence of the coating.

The following **Table 1** shows the most frequently-repeated value for each sample.

This indicates that particle size has been increased by around 40 times.



**Figure 1.** SEM photographs of (a) LAA uncoated ( $\times 265$ ) and (b) LLA coated ( $\times 280$ ).



**Figure 2.** Size distribution.

**Table 1.** Most frequently-repeated value in the data set.

LAA uncoated	10.39 µm
LAA coated	429.19 µm

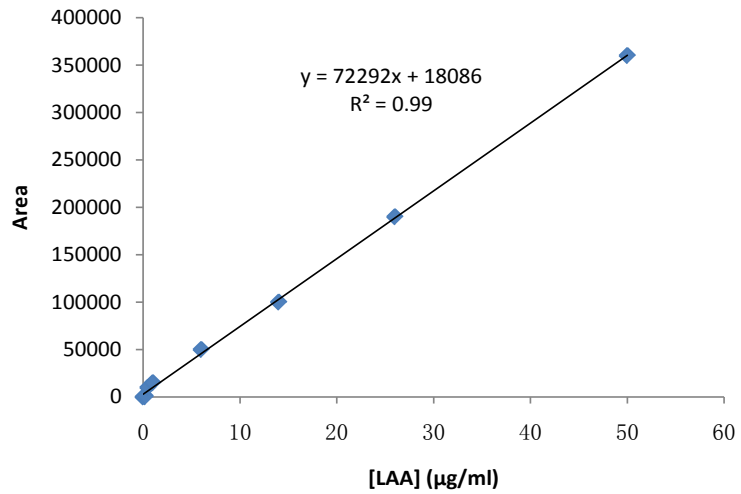
### 4.3. Determination of LAA in the Microcapsules by Chromatography

The calibration curve is shown in **Figure 3**.

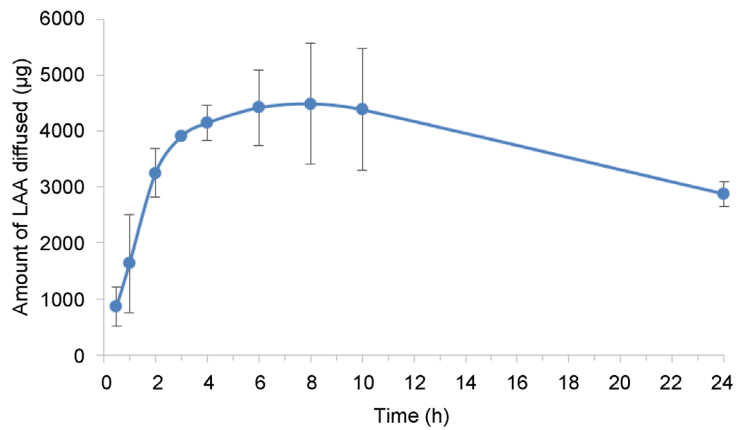
Coated ascorbic acid was determined by dissolving the sample in methanol and a buffer solution of phosphate, pH 7.4. The result is  $60.14\% \pm 1.37\%$  referring to the weight of dry-powder weight of the microparticles.

### 4.4. Trans-Membrane Diffusion Trial

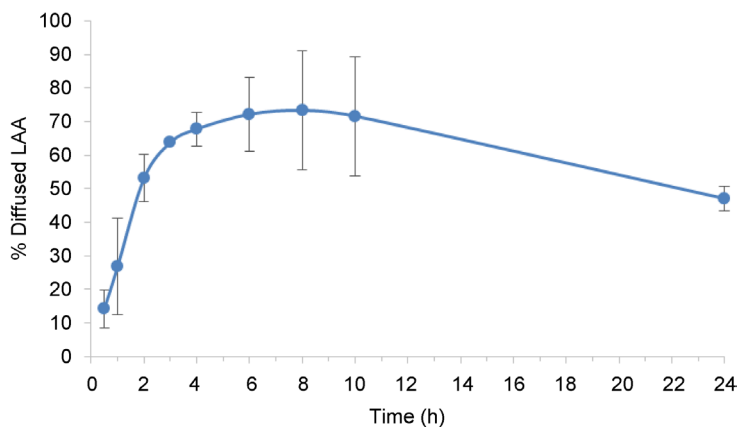
The resulting diffusion profiles expressed as a total accumulated quantity and as an accumulated percentage are shown in **Figure 4** and **Figure 5**.



**Figure 3.** Ascorbic acid calibration curve.



**Figure 4.** Accumulated ascorbic acid quantities diffused through the microcapsules (average values after two repetitions).



**Figure 5.** Accumulated ascorbic acid percentages diffused through the microcapsules (average values after two repetitions).

As can be seen in the above graphs, the coating dissolves upon contact with the pH 7.4 buffer solution, releasing LAA which diffuses rapidly through the membrane: in two hours, more than 50% of the LAA has diffused.

The reduction in concentration observed after 10 hours may be related to the instability of the ascorbic acid in the medium [14] [15]. Therefore, L-ascorbic acid degrades unavoidably in aqueous solution [16].

## 5. Conclusions

Ascorbic acid, or Vitamin C, is an essential nutrient in the development and repair of tissue, as well as being an antioxidant which slows down the ageing process caused by the damage from free radicals.

The instability of ascorbic acid has led to the use, in cosmetic products, of more stable derivatives which do not oxidise so readily.

Coating ascorbic acid particles protects them from oxidation and permits slow release upon contact with the skin, making it an ideal formulation for use in cosmetic products.

Coating of LAA using a fluid bed and a polymer control release pH dependent as the coating was feasible for obtaining a protective coating. The microparticles showed high encapsulation efficiency and excellent performance with respect to LAA protection.

The experiment in which the slow release of LAA was determined under strict pH conditions demonstrates the ability of LAA to be released from microparticles and absorbed by the skin.

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