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Osmotic-driven mass transport of water: Impact on the adhesiveness of hydrophilic polymers

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ABSTRACT

Adhesion is an important property for the functionality of many medical devices. One reason for the development of adhesive forces is dehydration caused by mass transport of water. Osmotic pressure is one main driving force for mass transport and the correlation between osmotic pressure and adhesive force has not been studied yet, which was the aim of the present study. A model system was used where a Carbopol tablet was lowered onto a 1% (w/w) agarose gel. The force required to detach the tablet (adhesive force) and the weight gain of the tablet (as a measure of transported water) were determined. Sodium chloride and mannitol were added to the agarose gel to decrease the osmotic pressure difference between the agarose gel and the partially hydrated Carbopol tablet. This resulted in a decrease of both mass transport and adhesive force. In addition, experiments with restricted water transport within the agarose gel were performed by preparing gels with different agarose concentrations. An increase of the agarose concentration resulted in decreased water transport and higher adhesive forces. Hence, the results confirmed our hypothesis that osmotic-driven mass transport and restricted mass transport of water correlate very well with the adhesive force.

1. Introduction

In the middle of the 20th century various hydrocolloids were explored to become "sticky" materials when they are hydrated by water [1]. These properties promised advantages in several medical and pharmaceutical fields. Due to the ability of hydrocolloids to stick to a surface, they have since then been used in the development of different medical devices such as bandages, dressings, patches, dental adhesives, and mucoadhesive formulations [2–6]. Many studies have been carried out on the attachment of materials to biological tissues, also referred to as bioadhesion [7]. Various *in vitro* methods have been developed to study the mechanisms behind the process of bioadhesion, to investigate factors influencing the adhesive strength, and to characterize the adhesive properties of different materials [3–13]. Several of these studies have shown the importance of water transport on the adhesion process [8–10]. Already in 1965, Kanig and Manago-Ulgado studied water absorption by ointments in correlation to the adhesive strength [11]. In the last decades, the development of adhesive formulations for mucosal drug delivery has led to a variety of studies in the process of mucoadhesion, which is defined as bioadhesive interactions with mucosal surfaces [12]. Mortazavi, Smart, and co-workers studied water movement from a mucus gel to various dry mucoadhesive materials and could show that hydration of dry materials correlated both to the dehydration of the mucus gel and to the corresponding adhesive forces. They also concluded that water transport is an important factor in bioadhesion of hydrophilic polymer materials to wet surfaces [9,13,14].

It is well known that one main driving force for mass transport of water, in addition to gravitation and mechanical forces such as pressure, is a difference in the chemical potential, μ. The nature strives for compensating this difference and an increasing gradient in chemical potential leads to enhanced mass transport (J). Mathematically, this can be expressed as

$$J \approx -D\frac{\delta\mu}{\delta x} \approx -D\frac{\delta\pi}{\delta x} \tag{1}$$

where D is the mutual diffusion coefficient, x the distance, and π the osmotic pressure. The osmotic pressure of a system is defined by the relation [15]

$$\pi = -\frac{1}{v_1}(\mu_1 - \mu_1^{\circ}) \tag{2}$$

where μ_1 is the chemical potential of the solvent in the system, μ_1° is the chemical potential of pure solvent, and v_1 is the molar volume of the solvent. Thus, as can be seen from Eq. (1), a gradient in the chemical potential or in the osmotic pressure (Eqs. (1) and (2)) will govern mass transport of the pure solvent.

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Although difference in chemical potential, or expressed in terms of osmotic pressure, is one main driving force for mass transport, no study has been published that relates the adhesive force to osmotic pressure gradients. However, this is of great interest for the functionality of adhesive medical devices and the possibilities of developing efficient bioadhesive medical devices. Lejoyeux et al. published a study in 1989 on the influence of the ionic strength of the test medium on the adhesive force of a polyacrylic acid tablet. They changed the ionic strength of buccal mucosa by addition of sodium chloride (NaCl) and observed a loss of bioadhesion with increasing NaCl concentration [16]. However, they did not discuss the results in terms of osmotic pressure effects. Following the theory of mass transport, the extent of the osmotic pressure difference will affect mass transport of water from the test medium into the adhesive tablet. Our hypothesis is that this mass transport will correlate with the generated adhesion force. To establish such a general correlation is of fundamental interest within the bioadhesion area. In order to be able to investigate this hypothesis a model system needed to be developed where the differences in osmotic pressure can be altered. The chosen model system (Fig. 1) consisted of a compressed dry polyacrylic acid (Carbopol) tablet and an agarose gel containing large amounts of water (about 99% (w/w)). Mortazavi and Smart used a similar system in a study where different polymeric tablets wrapped into dialysis tubing were attached to a mucus gel and the resulting dehydration of the mucus gel was studied [13]. They showed that mass transport of water occurred from the mucus gel into the polymer, which caused a local dehydration of the mucus gel. However, they did not correlate the osmotic effect to mass transport nor to the adhesive force, although the observed dehydration may be one possible reason for the suction of the tablet to the gel surface [13,14].

In the model system used in the present study, a Carbopol tablet is lowered onto an agarose gel, leading to a partial hydration of the tablet and the suction of the tablet onto the surface of the agarose gel. The adhesive force can then be characterized by measuring the detachment force needed to separate the Carbopol tablet from the agarose gel (see Fig. 1). The aim of this study was to prove the hypothesis that changes in the osmotic pressure difference will generate differences in mass transport, and that this mass transport correlates with the developed adhesive force. For this purpose, sodium chloride and mannitol were added to the agarose gel in the model system in order to tune the osmotic pressure of the agarose gel. In addition, the effect of restricted mass transport in the agarose gel was studied to further investigate the correlation of mass transport and adhesive force. Agarose gels with different concentrations of agarose were prepared in order to change the ability for water transport within the agarose gel and the effects on both mass transport and adhesive force were investigated.

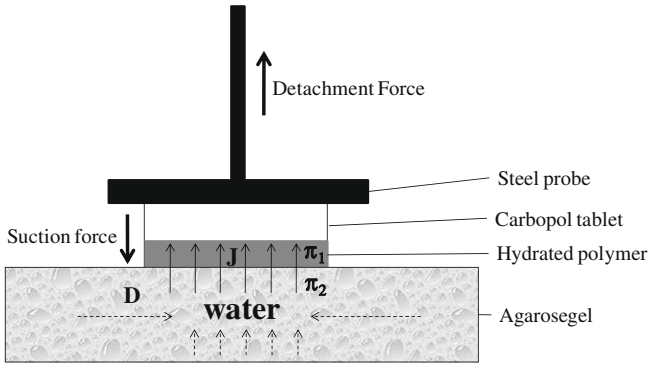

Fig. 1. Schematic picture of the model system. Mass transport of water occurs from the agarose gel into the partially hydrated Carbopol tablet controlled by the mutual diffusion constant (D) and the differences in osmotic pressure (π_1 and π_2).

2. Materials and methods

2.1. Materials

Carbopol 974-P NF (cross-linked polyacrylic acid) containing maximum 2.5% sulfated ash was obtained from Noveon (USA), and agarose (for electrophoretic routine use, ⩽1% sulfated ash) and D-mannitol were both from Sigma–Aldrich (Germany). Sodium chloride and magnesium stearate were purchased from Prolabo (France) and Peter Greven Fett-Chemi (Germany), respectively, and ethanol 99.7 vol.% (Etax) was from Altia Corporation (Finland). Sodium dihydrogen phosphate monohydrate and disodium hydrogen phosphate dehydrate from Fluka Chemie (Switzerland) were used for the preparation of the buffer solutions. All chemicals were of analytical grade and were used as received.

2.2. Preparation and characterization of test tablets

For the preparation of the Carbopol test tablets a single punch hydraulic press (PELA 15 ton shop press, China) was used. Tablets were prepared by direct compression of 350 mg Carbopol at 130 MPa using 12 mm diameter flat-faced dies. The walls of the die were lubricated with magnesium stearate dissolved in ethanol before use. The powder was weighed on an analytical balance and manually filled into the die.

The average weight and height of the tablets were determined from 10 tablets to 355 ± 9 mg and 2.5 ± 0.1 mm, respectively. Diametral compression tests were performed (Schleuniger AM, Germany) according to Fell and Newton [17] in order to determine the force needed to fracture the tablets. The radial tensile strength of the tablets (σ) was calculated according to

$$\sigma = \frac{2F}{\pi D h} \tag{3}$$

where F is the fracture force (N), D is the tablet diameter (mm), and h is the tablet height (mm).

The apparent particle density for Carbopol 974-P NF was measured using a helium pycnometer (AccuPyc 1330 Micromiretics, Chemical Instruments AB, Sweden). Three samples were taken from the powder and each sample was measured ten times with an automatic procedure. The theoretical porosity, E (%), of the tablets was calculated according to

$$E = \frac{\pi r^2 h - \left(\frac{m_{tot}}{\rho}\right)}{\pi r^2 h} \tag{4}$$

where r is the radius of the tablet (cm), h is the tablet height (cm), m_{tot} is the total weight of the tablet (g), and ρ is the apparent density for Carbopol (g/cm^3).

2.3. Preparation of agarose gels

A mixture of agarose powder and Milli-Q water was heated under stirring until boiling. The hot solution was casted into steel vessels (6 ml in each vessel) which were immediately covered with a plastic lid to avoid evaporation. The solution was allowed to cool down and gel for 10 min. The resulting gels had a diameter of 5 cm and an average height of 3.1 ± 0.2 mm. To avoid dehydration of the gel surface, 2 ml water was added onto the stiff gels. This water was removed prior to the measurements.

2.4. Adhesion experiments

All adhesion tests were performed at room temperature using a TA-HD*i* Texture Analyzer (Stable Micro Systems, UK) with a 5 kg loading cell. The Carbopol tablets were glued on a steel probe