

Instrumental drug analysis

Exercise 5

Wettability properties of polymeric materials

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Introduction

The potential of using intact skin as the route of drug administration has been known for several years. The inspiration of using skin for delivery of drug is from ancient time. Historically, the medicated plaster can be viewed as the first development of transdermal drug delivery systems (TDDS) [1].

TDDS is a combinational product i.e. a combination of a drug and a device to administer the drug into the biological system. TDDS is made up of polymeric materials. There are some polymers that are used as adhesives, some as backing membrane and some as release liner for the fabrication design of transdermal patch. Every layer in the TDDS requires specific properties for that layer only. The type of polymers are chosen according to the desired properties for that specific layer. The physical properties and the polymer materials showing those properties are listed below [1]:

- Polyurethane for elasticity,
- Polysiloxanes for insulating ability,
- Poly(methyl methacrylate) for physical strength and transparency,
- Poly(vinyl alcohol) for hydrophilicity and strength,
- Polyethylene for toughness and lack of swelling,
- Polyvinylpyrrolidone for suspension capabilities.

The other types of polymer are those that are desired for the controlled release of the drug. The polymers that are currently used in the manufacturing of the TDDS are poly(2-hydroxyethyl methacrylate), polyvinylpyrrolidone, poly(methyl methacrylate), poly(vinyl alcohol), poly(acrylic acid), polyacrylamide, poly(ethylene-co-vinyl acetate), polyethylene glycol, poly(methacrylic acid) [1].

Transdermal patches and medicated plasters are pharmaceutical preparations designed to provide a prolonged delivery of drugs to the skin to achieve a systemic or local effect, respectively. Usually, they are drug-in-adhesive systems, in which the drug is dispersed and/or dissolved in a pressure-sensitive adhesive (PSA) matrix. PSAs are defined as soft polymeric materials that display an instantaneous adhesion on almost any surface by simple contact under a light pressure and that can ideally be detached from the substrate without any residue [2]. The efficiency of the therapeutic treatment by these dosage forms is related not only to their ability to release the drug through the skin, but also to their complete skin contact over the whole delivery surface for the entire treatment period. If the patch lifts or partially detaches, the effective contact area, and thus the drug absorption, is unpredictable and therapeutic failure can occur. The adhesion properties of a PSA strongly depend on their viscoelastic properties. Viscoelastic materials are needed in order to relax stresses, easily create a molecular contact, and dissipate energy upon debonding [2]. Every TDDS needs to be applied to the skin and kept in place for several hours and in some cases even days.

It is important to understand the fundamentals of skin before deciding on the polymers that can be used as adhesives. The measured surface energy of the adhesive must be equal to or less than that of the adherend, or human skin in this case. The other fundamental conditions that need to be addressed are kinetic requirement involving wetting rates and visco-elastic nature of the adhesives. These are important to know because the skin has water content which may react with the polymeric adhesive making the bond between the skin and the patch [1].

Wettability studies usually involve the measurement of contact angles as the primary data, which indicates the degree of wetting when a solid and liquid interact [3]. Contact angle measurements are often used to evaluate surface and liquid cleanliness and the effects of surface treatments developed as a part of fundamental research in surface science, as well as for industrial applications [4]. Small contact angles (90°) correspond to high wettability, while large contact angles (90°) correspond to low wettability [3].

The contact angle is defined as the angle formed by the intersection of the liquid-solid interface and the liquid-vapor interface (geometrically acquired by applying a tangent line from the contact point along the liquid-vapor interface in the droplet profile). The interface where solid, liquid, and vapor co-exist is referred to as the “three phase contact line”. Figure 1. shows that a small contact angle is observed when the liquid spreads on the surface, while a large contact angle is observed when the liquid beads on the surface [3].

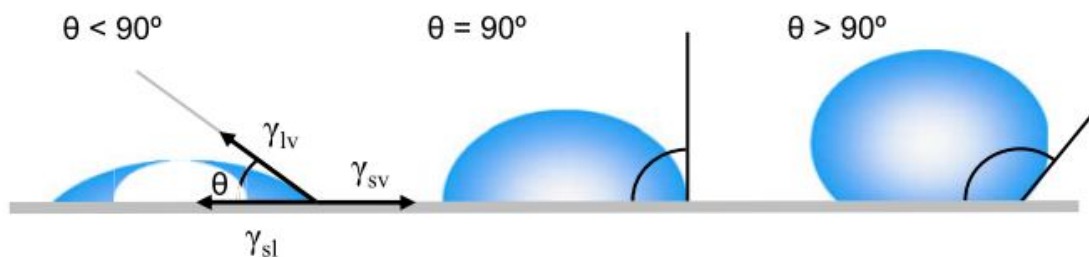


Fig. 1. Illustration of contact angles formed by sessile liquid drops on a smooth homogeneous solid surface [3].

Ideally, the shape of a liquid droplet is determined by the surface tension of the liquid. In a pure liquid, each molecule in the bulk is pulled equally in every direction by neighboring liquid molecules, resulting in a net force of zero. However, the molecules exposed at the surface do not have neighboring molecules in all directions to provide a balanced net force. Instead, they are pulled inward by the neighboring molecules (Fig. 2), creating an internal pressure. As a result, the liquid voluntarily contracts its surface area to maintain the lowest surface free energy. From everyday life, we know that small droplets and bubbles are spherical, which gives the minimum surface area for a fixed volume. This intermolecular force to contract the surface is called the surface tension, and it is responsible for the shape of liquid droplets. In practice, external forces such as gravity deform the droplet; consequently, the contact angle is determined by a combination of surface tension and external forces (usually gravity). Theoretically, the contact angle is expected to be characteristic for a given solid-liquid system in a specific environment.



Fig. 2. Surface tension is caused by the unbalanced forces of liquid molecules at the surface [3].

As first described by Thomas Young in 1805, the contact angle of a liquid drop on an ideal solid surface is defined by the mechanical equilibrium of the drop under the action of three interfacial tensions (Fig. 1):

$$\gamma_{lv} \cos \Theta_Y = \gamma_{sv} - \gamma_{sl} \quad (1),$$

where γ_{lv} , γ_{sv} , and γ_{sl} represent the liquid-vapor, solid-vapor, and solid-liquid interfacial tensions, respectively, and θ_Y is the contact angle. (1) is usually referred to as Young's equation, and θ_Y is Young's contact angle.

The solid surface with a surface energy that is higher than the surface tension of a liquid drop will undergo complete wetting so that adhesiveness dominates, and the drop spreads such that the contact angle is 0° . This can be illustrated by the complete spreading of water on any substrate that has a higher surface energy than that of water itself (i.e., $> 72.8 \text{ mN m}^{-1}$, water surface tension). If the substrate has a relatively high surface energy, yet lower than the liquid's surface tension, the liquid will wet the solid surface and the resulting contact angle is $0^\circ < \theta < 90^\circ$. Conversely, if the surface energy of the solid surface is low, it will undergo poor wetting and poor adhesiveness of the drop, resulting in a larger contact angle. For example, a water drop that has a contact angle $>90^\circ$ is characterized as non-wetting, and the solid surface is said to be hydrophobic (see Fig. 1).

Measuring contact angles with a high level of precision usually requires high-tech contact angle goniometers.

Values of the static contact angle (determined by the method of dropped droplets in which the single drop is putted on the solid surface and the optical measurement) are strongly dependent on:

- the time intervals between the putted drops and the measurements,
- volatility of the solvent
- the adsorption process on the surface of solid phase (for porous materials)
- and other interaction on the surface.

The one of the most commonly used method of calculation the free energy of the surface (γ_s) is the Owens'-Wendt's method, which assumes that this energy is the sum of components dispersion (γ_s^d) and polar (γ_s^p) interactions (see Eq. 2)

$$\gamma_s = \gamma_s^d + \gamma_s^p \quad (2).$$

In this method for both parts it is necessary to used two liquids with the well known the values of both components: (γ_s^d and γ_s^p) and resolve the appropriate system of equations 3 and 4:

$$\sqrt{\gamma_s^d} + a\sqrt{\gamma_s^p} = b(1 + \cos \Theta_1) \quad (3),$$

$$\sqrt{\gamma_s^d} + c\sqrt{\gamma_s^p} = d(1 + \cos \Theta_2) \quad (4),$$

where coefficients a , b , c and d depend on the type of the liquid, which are calculated directly from values of the dispersion component and polar component, and angles \square_1 and \square_2 are the contact angles of the selected liquids used during the measurements. This selected liquids should be selected to differ significantly with the dispersion and polar components. The typical pair of solvents is water (W) and diiodomethane (D). For this pair the transformation of the Eq. 3 and 4 it can be obtained the components of free surface energy for solid (see Eq 5 and 6):

$$\gamma_S^d = \left[\frac{\gamma_D (\cos \theta_D + 1) - \sqrt{\frac{\gamma_D^p}{\gamma_D} \gamma_W (\cos \theta_W + 1)}}{2 (\sqrt{\gamma_D^d} - \sqrt{\gamma_D^p \frac{\gamma_W^d}{\gamma_W^p}})} \right]^2 \quad (5),$$

$$\gamma_S^p = \left[\frac{\gamma_W (\cos \theta_W + 1) - 2 \sqrt{\gamma_S^d \gamma_W^d}}{2 \sqrt{\gamma_W^p}} \right]^2 \quad (6).$$

Experimental

1. The tutor will select the type of membranes which will be used during laboratory it could be: polyethylene, Teflon, poly(vinyl chloride) polypropylene, polyamide 6, etc.
2. The surface of membrane should be washed with the methanol before measurement.
3. On the clean surface of selected membrane put using Goniometer PGX the droplet of water and measure the contact angle according to the using instruction of the aperture. The obtained values should be similar until you will receive 10 similar values.
4. After measuring the contact angles for water for all selected membranes in the next step the contact angles for diiodomethane should be performed in the same ways as for water.
5. In the next part the plasma modification of selected membranes will be performed according to the instructions given by the tutor and the contact angles for water should be measure again after modification.
6. Calculate the energy of all using membranes, using the program for the calculated the surface energy. For the comparison, calculate the free surface energy using the Owens'-Wendt's method. The average values of contact angle should for both solvents be used for all calculations. The values of the components do water and diiodomethane are given in the Table 1.

Table 1. The values of contents for water and diiodomethane

Solvent	γ	γ^d	γ^p
Water	72.8	51.0	21.8
Diiodomethane	50.8	48.5	2.3

Issues:

1. The surface tension – the definition and the basic information
2. The types of interactions in polymers
3. Adhesion and cohesion
4. The contact angle

Report should contain:

The table with all results please mark the values which were taken to the calculations, the calculated values of the surface energy and analysis of results in the context of structure of selected polymers.

References:

- [1] S. Banerjee , P. Chattopadhyay, A. Ghosh, P. Datta, V. Veer, *Aspect of adhesives in transdermal drug delivery systems*, International Journal of Adhesion & Adhesives, 50 (2014) 70–84.
- [2] G. M.G. Quaronia , Ch. G.M. Gennaria , F. Cilurzoa , G. Ducouretb , C. Cretonb, P. Minghettia, *Tuning the rheological properties of an ammonium methacrylate copolymer for*

the design of adhesives suitable for transdermal patches, European Journal of Pharmaceutical Sciences, 111 (2018) 238-246.

[3] Y. Yuan, T. Randall Lee, Contact Angle and Wetting Properties Chapter 1
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[4] Guillaume Lamour and Ahmed Hamraoui, Contact Angle Measurements Using a Simplified Experimental Setup

https://www.temple.edu/borguet/Publication/Documents/pdf_files/2010-7.pdf