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Relationships between surface free energy, surface texture parameters and controlled drug release in hydrophilic matrices

J. Saurí [a,b,*], J.M. Suñé-Negre [a,c], J. Díaz-Marcos [d], J. Vilana [d], D. Millán [e], J.R. Ticó [a,c], M. Miñarro [a,c], P. Pérez-Lozano [a,c], E. García-Montoya [a,c]

[a] Pharmacy and Pharmaceutical Technology Department, Universitat de Barcelona, Barcelona, Spain
[b] Recipharm, Parets del Vallès, Barcelona, Spain
[c] IDIBELL-UB Research Group: Pharmacotherapy, pharmacogenomics & Pharmaceutical Technology, Barcelona, Spain
[d] Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB), Barcelona, Spain
[e] Lab. Kern Pharma, Barcelona, Spain

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ABSTRACT

The study of controlled release and drug release devices has been dominated by considerations of the bulk or average properties of material or devices. Yet the outermost surface atoms play a central role in their performance. The objective of this article has been to characterize the surface of hydrophilic matrix tablets using the contact angle (CA) method to ascertain the surface free energy, and atomic force microscopy (AFM) and confocal microscopy (CM) for the physical characterization of the surface of the hydrophilic matrix. The surface free energy results obtained show that hydroxypropylmethylcellulose K15M hinders the spreading of water on the surface of the tablet, such that the concentration of HPMC K15M increases the reaction rate of the hydrophobic interactions between the chains of HPMC K15M which increases with respect to the rate of penetration of water into the tablet. In this study, we developed a new method to characterize the swelling of the tablets and established a relationship between the new method based on microswelling and the swelling ratio parameter. The surface texture parameters have been determined and the morphology of the tablets of the different formulations and the evolution of the surface morphology after interacting with the water, swelling and forming a gel layer were characterized. This work represents significant progress in the characterization of matrix tablets.

1. Introduction

Characterization methods for tablet surface in the micro- and nanometre range are discussed for the characterization of Captopril hydrophilic matrices, including atomic force microscopy (AFM), confocal microscopy (CM), and contact angle.

Analysis of surface topographic measurements produces roughness parameters, such as, root mean square roughness and arithmetic average roughness (Poon and Bhushan, 1995). These parameters have been previously shown to correlate with the mechanical properties (brittle/ductile tendencies and elasticity) of compacted materials (Narayan and Hancock, 2003). Other useful examples of surface texture studies for pharmaceutical applications include the analysis of tablet film coatings for the inspection of defects (Ruotsalainen et al., 2003), the inspection of punches for sticking problems (Roberts et al., 2003), and drying effects on the compaction behaviour of pellets (Bashaiwoldu et al., 2004).

Surface roughness influences particle flow properties, wettability, friability, coating processes and particle–particle interactions. Confocal microscopy and atomic force microscopy provide quantitative roughness data on two different scales, confocal microscopy from 1 mm and atomic force microscope from the 100 μm scale.

Confocal microscopy (CM) is an accurate, quantitative, and flexible method that can be used to study areas with diameters of up to several centimetres. Optical measurements collected by the microscope head formulate a detailed map of the sample surface by combining the path of light reflecting off the surface with the light reflected off the reference surface. Then a computer image of the surface with the corresponding exact dimensions of the surface is generated. The resolution of this method is dependent on the objective implemented, which is below the micrometre range.

Atomic force microscopy (AFM) was invented by Binning et al. (1986) and is a direct method for determining the topography of

* Corresponding author at: Pharmacy and Pharmaceutical Technology Department, Universitat de Barcelona, Avda. Joan XXIII s/n, 08028 Barcelona, Spain. Tel.: +34 934034712; fax: +34 93404546.
E-mail address: jaumesauri@hotmail.com (J. Saurí).

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3-D conducting and insulating surfaces, in some cases with atomic resolution. In AFM the sample is scanned by a tip, which is mounted to a cantilever spring. While scanning, the force between the tip and the sample is measured by monitoring the deflection of the cantilever. As the probe scans the sample surface, the mechanical force between the probe and the sample is measured. Alternatively, it is possible to plot the height position of the translation stage. This height is controlled by a feedback loop, which maintains a constant force between tip and sample. Lateral resolution is determined and limited by the sharpness of the probe used. The tip diameter is in the nanometre range (about 8–10 nm).

Knowledge of the wettability and surface free energy of pharmaceutical solids is important in the rational design of pharmaceutical formulations. Information of this type can provide indications as to interfacial interactions and compatibility among formulation components. Many phenomena of pharmaceutical importance initiate at the surface, and can be critically affected by surface behaviour. Amongst these, solid–liquid interfacial interactions are of special interest as they can have a direct implication on drug dissolution and stability.

Various techniques are employed to assess the wettability and surface energy of powders, such as the contact angle method, the floatation method, isothermal microcalorimetry, and inverse gas chromatography (IGC). The contact angle method (CA) via sessile drop is a commonly used method for obtaining surface energy data, with which interactions between materials can be estimated (Zhang et al., 2002). Contact angle methods to probe surface properties are highly surface sensitive, low cost, readily performed in most laboratories, and reasonably easy to understand. In the simplest configuration, a small drop of a pure liquid of known surface tension is placed on the solid surface to be measured. The angle of a tangent to the drop profile originating from the point of contact of drop and surface is measured. The angle through the fluid phase is, by convention, the value reported. The angles measured are influenced by the purity of the measurement liquid, the penetration of the liquid into the substrate, sample roughness, drop size, surface swelling and a number of other factors (Ratner and Kwok, 1999).

Particle wetting is a prerequisite for processes such as disintegration, dispersion, dissolution and solubilisation, and is primarily governed by powder surface energetics. However, powders are complex systems and can exhibit heterogeneous surface properties (Puri et al., 2010). The importance of contact angles and wettability on dissolution rate has been reported in several studies (Brown et al., 1998; Buch et al., 2011; Lippold and Ohm, 1986; Tian et al., 2007).

Penetration of water into tablets or into granules precedes dissolution. The wettability of the powders, as measured by the contact angle of the substance with the solvent, therefore determines the contact of solvent with the particulate mass. The measurement of the contact angle gives an indication as to the nature of the surface. The behaviour of crystalline materials can be related to the chemical structure of the materials concerned. There are many situations in which the wetting of surfaces is important, not only in the action of surfactants in aqueous media wetting hydrophobic drugs, but also in the case of polymer solution droplets spreading on tablet cores during spray drying. The type of wetting that occurs when a liquid spreads over a solid surface is referred to as spreading wetting. The tendency for spreading is described by the spreading coefficient (S), which for spontaneous spreading should be positive or zero. If S is negative, only limited spreading is obtained. The value of the spreading coefficient depends on the contact angle; complete wetting occurs when the contact angle is zero (Florence and Attwood, 2011).

Surface free energy is an important physicochemical property of a solid that can be assessed indirectly from wettability measurements. The ability to quickly form a continuous gelified barrier is related to the hydrophilicity of the polymer, therefore the surface free energy plays an important role in swelling kinetics (Rodriguez et al., 2000).

The objective of this article is to characterize the surface of the tablets determining the surface free energy and the surface texture parameters, and relate the surface free energy, the dynamic swelling and the dissolution rate in the different formulations. For the study, Captopril formulations have been developed using the methodology quality by design (ICH Q8) method.

2. Theoretical considerations

2.1. Contact angle, wettability and surface free energy

Wetting of a porous substrate may also be considered a dynamic phenomenon. The liquid penetrates through the pores and gives different contact angles depending on the complexity of the porous structure. The value of θ depends on the history of the system and whether the liquid is tending to advance across or recede from the solid surface. The limiting angles achieved just prior to movement of the wetting line (or just after movement ceases) are known as the advancing and receding contact angles, θ_A and θ_R, respectively (Tadros, 2005).

Fowkes (1964) noted that surface interactions could only occur between forces of similar type; for example no interaction due to permanent dipoles can take place across an interface between polar and non-polar materials. The same author proposed that the surface energy be considered as additives contributions from dispersion, hydrogen bonding and induction forces. However, it has become usual to consider just two contributions representing polar and dispersion forces. Polar forces include; hydrogen bonding, interactions between hydrogen ion donor and hydrogen ion acceptor (Bronsted–Lowry acid bases), and interactions between electron pair acceptors and electron pair donors (Lewis acid bases). Dispersion forces include; dipole–dipole (Keesom force), dipole – induced dipole (Debye force), and London forces. Dispersion forces are interactions between non-polar materials. These dispersion forces occur between all materials and are also termed van der Waals forces (Bukton et al., 1995):

$$\gamma^{TOT} = \gamma^{p} + \gamma^{d} \quad (1)$$

In the method of Wu (1973), solid-surface free energy can be assessed by contact angle measurement of two liquids of known polarity and can be assessed by solving two equations with two unknowns.

$$(1+\cos\theta)\gamma l = \frac{4(\gamma^{d}s \times \gamma^{d}l)}{(\gamma^{d}s + \gamma^{d}l)} + \frac{4(\gamma^{p}s \times \gamma^{p}l)}{(\gamma^{p}s + \gamma^{p}l)} \quad (2)$$

where γl is the liquid surface tension and γs the solid surface free energy (Planinsek et al., 2000).

The solvents commonly used to determine surface free energy are water and diiodomethane (see Table 1).

When the liquid drop adheres to the solid surface it forms a surface tension γ_{SL}. The work of adhesion (W_a) is the difference between the surface tensions of the liquid/vapour and solid/vapour and that of the solid/liquid.

Table 1
Surface tension of the solvents used for surface free energy determination.

Solvent	γ^{d} (mN/m)	γ^{p} (mN/m)	γ^{TOT} (mN/m)	Work of cohesion (mN/m)
Water	21.8	50.2	72.0	144.0
Diiodomethane	50.4	0	50.4	100.8