Influence of the Sebum and the Hydrolipidic Layer in Skin Wettability and Friction

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P. Humbert et al. (eds.), *Agache's Measuring the Skin*,
DOI 10.1007/978-3-319-32383-1_19

Keywords
Human skin • Wettability • Water contact angle • Hydrophobic/hydrophilic balance • Sebum • Hydrolipidic layer • Friction coefficient

1 Introduction

Water changes the properties of human keratin fibers existing in the skin, hair, and nails (Barba et al. 2010). Examples are the sorption of water by stratum corneum, the spreading of water and lipidic liquids which influences skin absorption, thermal loss, as well as transcutaneous pressure of water vapor, carbon dioxide, and oxygen (Agache et al. 2004). The production of a sweat/sebum emulsion can also be influenced by these interactions as well as the behavior and effect of topical drugs or cosmetics on the skin (Agache et al. 2004).

Frequent washing increases brittleness of the nail (Uyttendaele et al. 2003), and chronic wetting and drying of nails may cause lamellar dystrophy (onychoschizia) (van de Kerkhof et al. 2005). Brittle nails affect about 20 % of the population, and women are affected twice as frequently as men (Lubach et al. 1986). Hydrophobicity of soft tissue surfaces in the human body, including those of the human oral cavity, has been described for decades as playing an important role in many biological processes, like cellular adhesion (Barba et al. 2010), contact inhibition, elasticity (Agache et al. 2004), tissue membranes functions, intracellular structures (Uyttendaele et al. 2003), and adhesion of infectious microorganisms (van de Kerkhof et al. 2005). Generally, tissues with absorption/exchange functions or, indeed, lubrication tend to be more hydrophilic. On the other hand, tissues requiring protection against pathogenic microorganisms or acids tend to be hydrophobic (Lubach et al. 1986).

From a fundamental point of view, wetting is an important phenomenon, because of its diverse applicability in everyday life. Friction and lubrication are intimately coupled to wettability.

In this chapter, we will first treat human skin wettability by showing effects of some treatments and applications on wettability parameters. Secondly, the skin friction coefficient will be studied through the effect of the surfaces hydrophobic/hydrophilic balance (Ho/Hi).

2 Human Skin Wettability

Wetting refers to the contact between a solid surface and a liquid; it depends on intermolecular interactions. The degree of surface wetting is evaluated through the measurement of contact angle. The wetting of the surface is the best, if it has the minimum contact angle (θ). When θ = 0°, the surface wets completely; the opposite corresponds to θ = 180° (dewetting), and the partial wetting refers to θ ranging from 0 to 180° (Fig. 1).

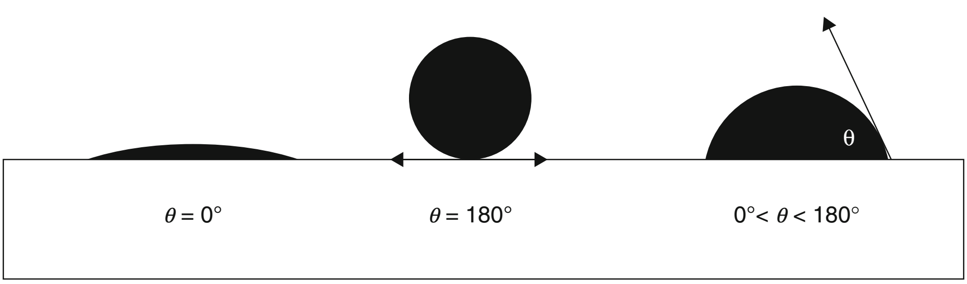


Fig. 1 Solid wettability: θ = 0°: total wetting, θ = 180°: non wetting = dewetting, 0° θ 180°: partial wetting, 0° < θ < 180°: partial wetting

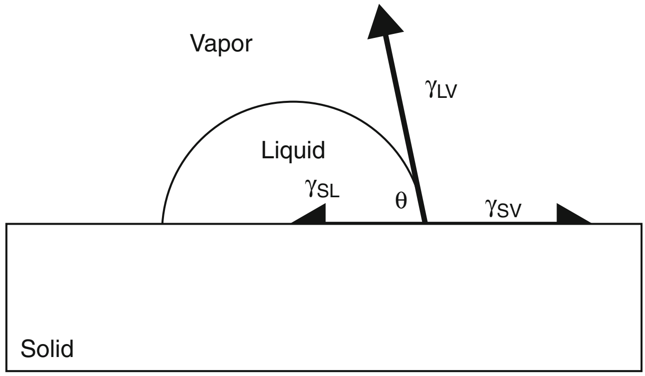


Fig. 2 Equilibrium of a liquid drop on a solid surface: contact angle and surface energy

2.1 Theory

2.1.1 Contact Angle and Superficial Energy (Fig. 2)

Young's equation (Eq. 1) (Young 1805) relates the surface tension between the liquid vapor (γ_{LV}), the solid vapor (γ_{SV}), and the solid-liquid (γ_{SL}) and the free surface energy by contact angle (θ). The general form of this equation for the solid-liquid-air system is

$$\gamma_{LV} \cos \theta = \gamma_{SV} - \gamma_{SL} - \pi_e \quad (1)$$

where π_e (external pressure) = 0 for low energy solids (Fowkes 1964).

2.1.2 Critical Surface Tension (γ_c) and Hydrophobic/Hydrophilic Balance (Ho/Hi)

Critical Surface Tension

γ_c (Fig. 3): The definition of γ_c is based on an empirical relationship between the cosine of the contact angle and the surface tension of a series of homologous liquid (Eq. 2) (Zisman 1964)

$$\cos \theta = 1 - b\left(\gamma_{liquid} - \gamma_c\right) \quad (2)$$

where γ_{liquid}, liquid surface tension (mJ/m^2). Note that a reduction of γ_c means an increase in the surface hydrophobia.

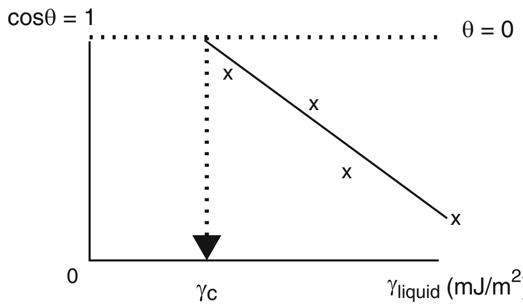


Fig. 3 Critical surface tension γ_c: total wetting condition (γ_{liquid} γ_c)

Hydrophobic/Hydrophilic Balance (Ho/Hi)

For decades, the surface hydrophobicity has been reported to play an important role in many biological processes, such as cellular adhesion, contact inhibition, elasticity, functionality of tissue membranes, functioning of intracellular structures, and adhesion of infectious microorganisms (Norris et al. 1999).

The skin hydrophobia balance (Ho/Hi) is quantified by a relationship between γ_c and the water surface tension (Eq. 3) (Elkhyat et al. 2001)

$$Hi = \gamma_c / \gamma_{H2O} \quad (3)$$

where Hi is surface hydrophilia and Ho is surface hydrophobia.

This parameter is expressed by the ratio of its critical surface tension γ_c to the water surface tension γ_{H2O} normalized by the latter.

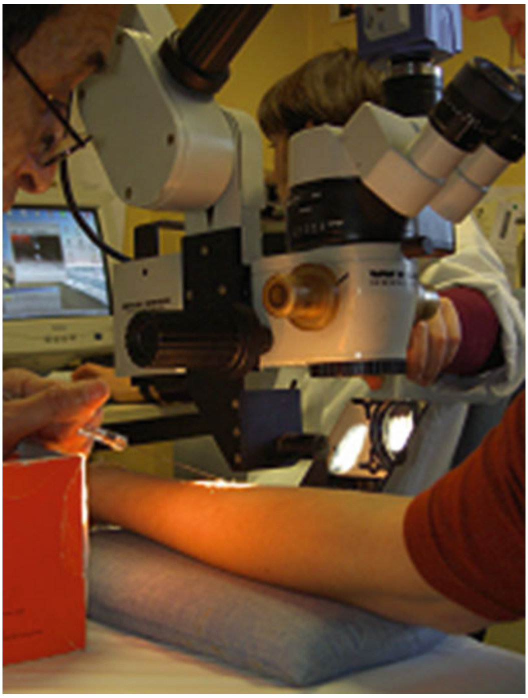


Fig. 4 Contact angle visualization and measurement: tool rests on the use of a mirror directed 45° to the skin "Profile drop method"

Free Surface Energy FSE (γ_s)

Free skin energy is a topical parameter that determines most of the surface properties such as adsorption, wetting, adhesion, etc. The γ_s of the solids cannot be directly measured, because of the very weak mobility of the molecular atoms. It is necessary to resort to indirect methods such as study of the interactions between a solid and a liquid. The γ_s is derived from the measurement of the contact angle of pure liquids, with known surface tension parameters.

Several approaches are mentioned in the literature; the two most commonly used for the skin are described below:

Geometric mean approach (Owens and Wendt 1969): The γ_s proportional to the intermolecular energy is the sum of the dispersion component γ_s^d and the polar component γ_s^p.

Acid-base approach (Van Oss et al. 1988; Good and Van Oss 1992): The γ_s can be expressed as the sum of Lifshitz-van der Waals γ_s^{LW} and acid-base γ_s^{AB} components $\gamma_s = \gamma_s^{LW} + \gamma_s^{AB}$. The acid-base components can be expressed as $\gamma_s^{AB} = 2\left(\gamma_s^+ . \gamma_s^-\right)^{1/2}$; the γ_s^+ and γ_s^- components indicate, respectively, the electron-acceptor and the electron-donor components.

2.2 Contact Angle Measuring

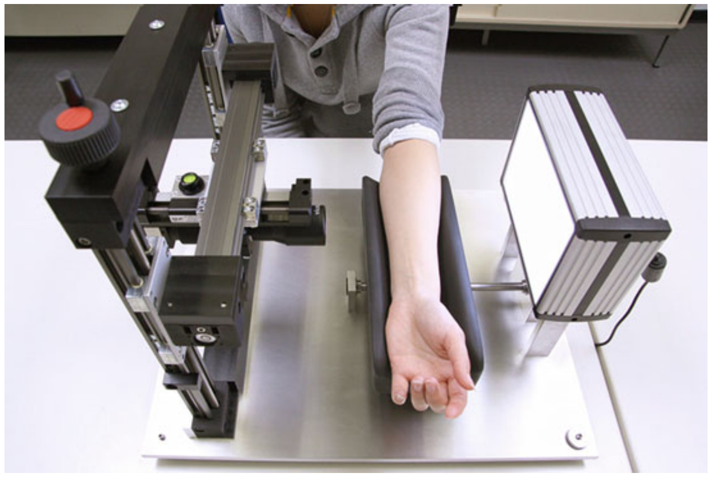
For the visualization and the measurement of the contact angle, we developed a tool especially designed for the wettability in vivo measurements (Fig. 4). This tool is based on the use of a mirror directed at a 45° angle to the skin (profile drop method).

A drop of test liquid is deposited on the skin surface using a microsyringe and inflated up to a final drop volume of 5 µl. The advancing contact angle of test liquids corresponds to the maximum value of the contact angle when the drop is inflated without moving the contact line.

The drop's image is recorded using a video camera (CDD-Iris, Sony, France) connected to a computer and mounted on a microscope (Wild Heerbrugg M650, Switzerland), with a magnification of ×16, fitted with a slanted mirror. After visualization and storage of the drop profile, the contact angle is measured using a program which can determine θ from the tangents of both sides of the drop. The influence of roughness and skin temperature on the contact angle is treated in the literature (Wenzel 1936; Neumann and Good 1979; Mavon et al. 1997). The temperature effects on the liquid in contact with the skin are minimized with the nature of the deposit (advancing contact angle) and with shortening the time of deposit (15–20 s).

In order to allow every researcher to be able to assess the skin wettability, a new device has just been developed which stands for drop shape analysis (Fig. 5). With this measuring procedure, a drop of liquid (mostly water) dribbled on the inner side of the lower arm. According to the wettability of the sample surface, the drop will take on a form depending on the surface tension. In order to interpret this form into a conclusive

Fig. 5 Human skin wettability measurement: forearm rest with the new device



value for measurements, the drop's contact angle is determined.

This device has three basic components: (1) A black and white camera with a telecentric measuring lens adjustable with a small linear axes portal. (2) An arm rest with adjustable settling angle. The angle is set to position the lower arm on which the measurement is performed as horizontal as possible. This setting prevents the drop to run or disintegrate, and both sides of the contact angles are the same on each side of the drop if the contact area is positioned horizontally. (3) Software: The software allows the adjustment of the arm in a horizontal position, the calculation of the drop angle, and saving of pictures and data.

2.3 Data Analyses

2.3.1 Water Contact Angle θ_w

Water is an important factor for normal skin function. When the water content decreases, the skin becomes dry, itchy, and uncomfortable. The spreading degree of a water drop on the skin surface is an indication of its hydrophobic (Ho) or hydrophilic (Hi) properties.

Skin: Water spreads differently on skin. On the volar forearm, a poor site in sebum, water forms a semi hydrophobic contact angle ($\theta_w = 80°-91°$) (Mavon et al. 1997; Elkhyat et al. 2004a, b; Schott 1971). On the forehead, rich site in sebum, water spreads over ($\theta_w = 57°-73°$) (Afifi et al. 2006; Fotoh et al. 2007; Mavon et al. 1998). A study of ten different sites (Afifi et al. 2006) was confirmed that the skin with poor sebaceous lipids is a hydrophobic surface ($\theta_w = 91°-102°$). On the rich sebaceous zones, the skin becomes hydrophilic ($\theta_w = 60°-85°$) (Fig. 6). Fotoh et al. (Fotoh et al. 2007) showed that the forehead skin wettability is significantly different ($p < 0.05$) between Black people (Africans or Caribbeans) ($\theta_w = 71°$) and Mixed races (African or Caribbean) ($\theta_w = 67°$) and Caucasians ($\theta_w = 67°$). The water contact angle θ_w was recently measured on the forehead of 60 children (aged 7–11), and the results showed a $\theta_w = 87°$ higher than adults indicating the skin is more hydrophobic than adults. Note that the sebum level measured on these children was particularly low (17 $\mu g/cm^2$) (Lodge 2007; Mac-Mary et al. 2012a).

Nail: The in vivo evaluation of the nails shows that human nail is a hydrophilic surface with a $\theta_w = 65°$ (Fig. 7). No significant difference has been found between different ethnicities (France, China, Iran, Morocco) or different sexes (Elkhyat et al. 2010).

2.3.2 Critical Surface Energy γ_c and Hydrophobic/Hydrophilic Balance (Ho/Hi)

The skin hydrophobia increases by decreasing γ_c. Just like θ_w, the critical surface tension (γ_c) values show that in the presence of sebum, the skin is less hydrophobic. On the forearm, γ_c is about

Fig. 6 Human skin wettability: effect of sebum on hydrophobic/hydrophilic balance

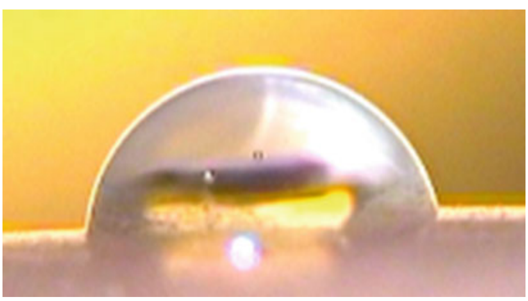


Fig. 7 Nail: hydrophilic surface with water contact angle = 65°

26–27.5 mJ/m^2 (Rosemberg et al. 1973; El-Shimi and Goddard 1973; Ginn et al. 1968; Adamson et al. 1968; Elkhyat et al. 1996), and on the forehead, as a rich site in sebum, γ_c increases (33.2 mJ/m^2) indicating an increasing of skin wettability. According to Eq. 3, the percentage of hydrophobia Ho of the forearm is between 62 % and 64 %, while the presence of sebum on the forehead reduces the skin hydrophobia to 54 %.

2.3.3 Surface Free Energy (γ_s)

The surface wettability increases with increasing γ_s.

The γ_s value of the skin at the forearm is approximately 38.5 mJ/m^2 (Elkhyat et al. 2001; Mavon et al. 1997), while on the forehead, it ranges between 42 and 46 mJ/m^2 according to the skin type (oily, normal, dry skin) (Mavon et al. 1998). The use of the acid-base approach shows that the forehead (sebum-rich area) is a strongly monopolar basic surface (γ_s^- = 26 mJ/m^2) and that the forearm (sebum-poor area) is a weakly basic surface ($\gamma_s^- = 4$ mJ/m^2) (Mavon et al. 1998). The γ_s increasing on the forearm is noticed by the increasing of the apolar component γ_s^{LW} (+10 mJ/m^2).

2.4 Effects of Some Treatments (Table 1)

The skin hydrophobia increases with the increase of θ_w and γ_c and decrease of γ_s (Elkhyat et al. 2001; Mavon et al. 1998).

2.4.1 Degreasing and Washing

Skin: Degreasing with organic solvents or washing with soap and water increases considerably the skin hydrophobia. This effect is observed by increasing the water contact angle θ_w (+10–15°) while reducing the free surface energy γ_s and the critical surface energy γ_c (Mavon et al. 1998). The initial skin hydrophilia of the forehead was found 2 h later after degreasing, time required for the reconstitution of the sebum current level (Mavon et al. 1998).

Nail: The degreasing of the nails with organic solvents also increases its hydrophobia (θ_w = +25°) (Fig. 8) (Elkhyat et al. 2010).

Hair: Virgin hair shows a mean thickness of 1.1 nm. The outermost layer of virgin hair surface is primarily made of a fatty acid called 18-methyleicosanoic acid (18-MEA), which strongly contributes to the hydrophobicity (θ_w = 103°) and lubricity of virgin hairs (Lodge 2007). Due to its hydrophobicity, the virgin hair surface is lacking of any water film, and therefore, the water film thickness measured on the surface is very low. Damaged hair, however, is slightly hydrophilic due to the removal of the fatty acid layer during damaging process (θ_W = 50°–80°) (Lodge 2007).

2.4.2 Application of Moisturizers (Cream, Thermal Water)

Our skin needs an adequate daily fluid intake to replenish the water stock in the dermis (dehydration will induce the loss of skin elasticity and increasing the skin folds). On the other hand, the skin should renew the hydrolipidic film essential for the appearance and also for the barrier function of the epidermis. Applying a moisturizer on the face of 60 children for 1 week showed a significant decrease in θ_w angle (−10°) indicating an increase in skin hydration (+15 arbitrary unit) (Mac-Mary et al. 2012a, b).

Table 1 Human skin wettability

	Volar forearm		Forehead	
	No treated	Degreasing "ether"	No treated	Degreasing "ether"
θ_w	80° (Wenzel 1936); 84° (Neumann and Good 1979) 88° (Fowkes 1964); 91° (Mavon et al. 1997)	92° (Neumann and Good 1979);101° (Fowkes 1964)	57–73° (Elkhyat et al. 2004b); 60° (Elkhyat et al. 2004a) 67–71° (Schott 1893–1895)	84° (Fowkes 1964)
γ_c	26 (Afifi et al. 2006); 26.8 (Fotoh C et al. 2007) 27 (Mavon et al. 1998); 27.5 (Lodge 2007; Mac-Mary et al. 2012a) 30.6 (Neumann and Good 1979)	21.6 (Mac-Mary et al. 2012a)	33.2	22.4
Ho	62 % (Elkhyat et al. 2001)	70 % (Elkhyat et al. 2001)	54 %	69 %
γ_s	38.5 (Fowkes 1964; Elkhyat et al. 2001)	32.4 (Fowkes 1964)	42–46 (Elkhyat et al. 2004b)	34.5 (Fowkes 1964)

θ_w: Water contact angle, Ho: Surface hydrophobicity; γ_c: Critical surface tension (in mJ/m^2); γ_s: Surface free energy (in mJ/m^2)

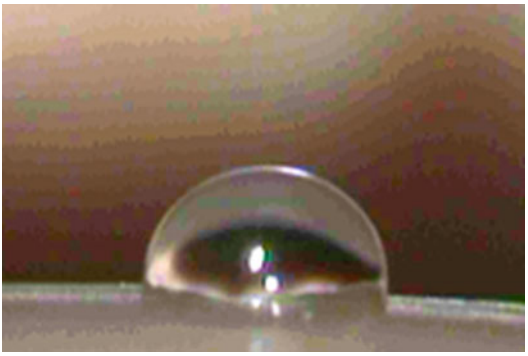


Fig. 8 Nail: degreasing effects: contact angle improvement (90°)

The effect of moisturizers is also noticed by increasing the critical surface energy (γ_c) and free surface energy γ_s. The application of thermal water reduces the skin hydrophobia by reducing the θ_w ($-10°$). This effect disappears 30 min after application (Elkhyat et al. 2004a).

2.4.3 Other Applications

Nutritional supplement provides comprehensive care of the skin envelope of the healthy individual and well-being as well. The effect of a nutritional supplement on the dryness in postmenopausal women has been shown with decreasing the contact angle which was initially hydrophobic (Humbert et al. 2005). The presence of mucus layer makes the surface of the pork tongue significantly more hydrophilic (more wettable). This effect is noted by decreasing the angle θ_w ($-27°$) and increasing the energy γ_s (+11 mJ/m^2) (Ranc et al. 2006).

2.5 Discussion

The skin wettability study shows clearly the role of hydrolipidic layer on the skin hydrophobia. The suppression or the alteration of this layer increases the skin hydrophobia. This capacity of the cutaneous lipids to increase skin wettability was attributed to the free fatty acids, especially to those existing in the sebum. By increasing the amount of squalene and paraffin in sebum, skin wetting was found to be increased (Gloor et al. 1973).

The in vivo quantification of physicochemical parameters of wetting nails has a potential value in the field of researches. The practical interest of drug penetration through transungual barrier function places these studies increasingly at the center of attention. The choice of intermediate films, including antifungals and varnishes, depends on the knowledge of these parameters.

3 Human Skin Friction Coefficient

The frictional behavior of the skin in contact with different materials plays a critical role in the sensory perception of them. The friction is extremely important in our perception of cosmetic application such as antiaging cream and moisturizers (Gee et al. 2005). The consumer exposure of the wide majority of cosmetic products is limited to dermal contact. While touching an object, a contact happens between our skin and the object; then the tribological properties of such a contact influence how an object is perceived. Sensory perception is an important factor in the decision-making process of consumers (Bongaerts et al. 2007).

The friction coefficient is the measurement of the level of sliding between two surfaces. The initial force to start the slide is called the "dynamic friction coefficient," while the force necessary to continue this is called the "kinetic friction coefficient." A high friction coefficient represents a weak slide, while a low friction coefficient indicates a good slide.

The review of the published literature on the skin friction shows a wide range of measured values of μ (Table 2). These differences indicate that the assessment of the friction coefficient of the skin is a highly complex problem. It involves skin elasticity, skin anisotropy, micro-topography, anisotropy of the skin relief leading to variation in testing conditions, and individual differences in measuring techniques. This last point can divide the test apparatus into two types of designs: one called incorporate linear motion, wherein a probe is pressed onto the surface and dragged across the skin in a straight line, and the other design is rotational and consists of a probe pressed onto

Table 2 Human skin friction coefficient (μ) – literature data

Author	Sliding material	Motion of test	μ	Ref
Comaish et al.	Teflon(1) nylon(2) polyethylene (3) wood(4)	Linear	0.2(1)–0.45(2)–0.3(3)–0.4(4) forearm	Comaish and Bottoms (1971)
Kenins	Different wool fabrics	Linear	0.32–0.48: dry skin	Kenins (1994)
			0.48–1.23: wet skin (forearm, finger)	
El-Shimi	Steel (rough[a], smooth[b])	Rotational	0.2–0.4[a]	El-Shimi (1977)
			0.3–0.6[b] (volar forearm)	
Highley et al.	Nylon	Rotational	0.19–0.28 (volar forearm)	Highley et al. (1977)
Cua et al.	Teflon	Rotational	0.34 (forehead)	Cua et al. (1990)
			0.26 (volar forearm)	
			0.21 (palm), 0.12 (abdomen)	
			0.25 (upper back)	
Asserin et al.	Ruby	Linear	0.7 (volar forearm)	Asserin et al. (2000)
Elkhyat et al.	Teflon(1)	Linear	0.18(1)–0.42(2)–0.74(3) (volar forearm)	Elkhyat et al. (2004b)
	Steel(2)			
	Glass(3)			
Elsner et al.	Teflon	Rotational	0.48 (volar forearm)	Elsner et al. (1990)
			0.66 (vulva)	
Sivamani et al.	Steel	Linear	0.56 (normal skin: dorsal finger)	Sivamani et al. (2003a)
			0.50 (isopropyl alcohol exposure: dorsal finger)	
			0.2 (normal skin in vitro)	
			0.3 (water exposed skin in vitro)	
Sivamani et al.	Steel	Linear	0.4–0.6 (volar forearm)	Sivamani et al. (2003b)
Derler et al.	Textile sample	Linear	0.27–0.7 (finger)	Derler et al. (2007)
Egawa et al.	Finger print		0.4 (volar forearm)	Egawa et al. (2002)
Lodén et al.	Steel	Rotational	0.55 (dorsum of the hand)	Lodén et al. (1992)
			1.1 (lower back)	
			0.65 (volar forearm) respectively in atopic skin	
			0.4 – 0.65 – 0.55	
Fotoh et al.	Steel	Linear	0.7–0.9 forehead	Fotoh C et al. (2007)

and rotated against the skin surface. The friction coefficient does not vary significantly with gender but varies considerably among the anatomical sites of the body (Cua et al. 1990; Elsner et al. 1990; Sivamani et al. 2003a); the age effect was also measured (Asserin et al. 2000; Elsner et al. 1990; Sivamani et al. 2003a). The friction coefficient is influenced by load (Asserin et al. 2000; Sivamani et al. 2003a; Koudine et al. 2000; Ramalho et al. 2007); however, it is increased due to water application (El-Shimi 1977; Asserin et al. 2000; Sivamani et al. 2003b). On the other hand, the application of petrolatum and glycerine on the forearm and on the hand decreases the friction coefficient immediately, and this effect lasts for at least 1 h after application (Ramalho et al. 2007). The application of isopropyl alcohol (Sivamani et al. 2003a) and washing with soap (Egawa et al. 2002) will dry the skin and decrease its friction coefficient. The finger has a friction coefficient (μ) ranged from 0.27 to 0.70 and varying among individuals due to different states of skin hydration (Derler et al. 2007). Recently, our group (Fotoh et al. 2007) showed a significant difference ($p <$ 0.05) of μ measured on the forehead depending on the ethnic affiliation. In 2004 (Elkhyat et al. 2004b), we showed the influence of the hydrophobic and hydrophilic characteristics of sliding and slider surfaces on μ. In this study, the wettability parameters for six surfaces (volar forearm, Teflon, silicone impression material [Silflo], vinyl polysiloxane impression material resin, steel, and glass) were measured, and their influences were compared to the friction coefficient μ.

The tribometer was developed and validated (Elkhyat et al. 2004b; Fotoh et al. 2007; Ranc et al. 2006; Asserin et al. 2000) to characterize the friction properties between skin in vivo and different sliding surfaces. A sliding ball of 10 mm diameter was pressed on the ventral forearm with a constant normal load (F_N) of 0.1 N and then moved at a constant velocity of 0.5 mms^{-1}. In order to maintain surfaces as flat as possible, a short sliding distance of 10–15 mm was selected.

In this study, we showed that if the skin is rubbed against a hydrophobic surface such as Teflon, the friction coefficient (μ) is lower than when rubbed against a hydrophilic surface such as glass or steel: so the hydrophobic surfaces have the lowest friction coefficient.

4 Discussion

Frictional properties of human skin depend not only on the skin itself including its texture, suppleness, smoothness, and its dryness or oiliness (Lodén et al. 1992) but also on its interaction with external surfaces and the outside environment (Zhang and Mak 1999).

In this chapter, we saw the role of the skin hydrophobia in the skin friction coefficient. The largest hydrophobicity of the abdomen explains its lowest friction coefficient compared to the forehead measured by Cua et al. (1990). Water application decreases the skin hydrophobia and consequently increases its friction coefficient measured by Egawa et al. (2002) and Sivamani et al. (2003b). The decrease of μ after degreasing (isopropyl alcohol) (Sivamani et al. 2003a) or after washing with soap and water (Egawa et al. 2002) is quite normal; indeed, these treatments increase the skin hydrophobia (Table 1), while the increased skin hydrophobia with aging or in atopic skins leads to low μ as reported in the literature (Asserin et al. 2000; Lodén et al. 1992).

The role of the surface lipids was speculated as one possible factor contributing to the frictional properties of the skin, and the correlation between μ and the skin lipid content was evaluated: Cua et al. (1995) showed that the skin lipid content plays a role in the frictional properties of the skin. Moreover, in the skin, the friction resistance depends on hydrophilic and lipophilic elements present on the cutaneous surface. Fotoh et al. (2007) assumed that the hydrophilic/hydrophobic balance of the cutaneous hydrolipidic film is different between the different ethnic groups studied. Black women could have a decreased skin friction coefficient as well as an increased cutaneous hydrophobicity comparatively to Mixed-race and Caucasian women.

5 General Conclusion

The exploitation of these parameters should allow to classify the different types of the skin according to their affinity with water, which is of major importance in biology as in cosmetology. These data should also be possible to guide the cosmetic formulation to discriminate the emulsions which cannot spread properly on the skin. Investigation of skin frictional properties is relevant to several research areas, such as skin physiology, skin care products, textile industry, human friction-dependent activities, and skin friction-induced injuries (Zhang and Mak 1999). Friction of skin forms an integral part of tactile perception and plays an important role in the objective evaluation of consumer-perceptible skin attributes (Wolfram 1983).

6 Conclusion

In cosmetic researches, the structure and the physicochemical properties of the skin, the nail, and the hair are of great interest. Studies of physicochemical parameters of wetting the skin bring a new look at the interactions between the formulations and keratin (or skin).

Up to now, these parameters are known as a fundamental tool to orient better the formulations. An average of evaluating certain activities or medicated cosmetics and knowledge of the physicochemical parameters of wetting the skin surface can provide useful information in the field of hygiene, cosmetics, and topical medications.

To date, the study of bio-tribological properties of human skin has attracted much attention, which is attributed to its importance in human daily life. A good understanding of skin friction is generally believed to have not only the potential benefits for the performance of conducting tasks but also the prevention of pain and discomfort (for instance, a good understanding of the mechanism between skin and various materials could help in avoiding the chance of getting blisters on the foot) (Liu et al. 2013).

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