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THE INFLUENCE OF SKIN TEMPERATURE ON DERMAL-EPIDERMAL ADHERENCE: EVIDENCE COMPATIBLE WITH A HIGHLY VISCOUS BOND*

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ABSTRACT

The influence of skin temperature on dermal-epidermal adherence was investigated. The adherence was measured by eliciting suction blisters; blistering time was determined under controlled skin temperature. In the range of skin temperatures investigated (20°-43° C) the adherence decreases continuously with increasing temperature. Adherence is, approximately, an exponential function of temperature; an increase of skin temperature by 10° C decreases blistering time by a factor of about 4.

This type of relationship supports the hypothesis that epidermis and dermis are connected by a viscous bond. The strong influence of skin temperature suggests that a high viscosity is involved.

Previous observations on suction blisters suggested that the resistance offered by the skin against this type of separation is of a viscous nature [1]. This conclusion was based on the observation that, for a given skin region, blistering time is inversely proportional to the suction pressure applied. Such a relationship fits theoretical models in which a viscous resistance is the dominant factor. The model studies did not, however, identify the nature of the viscous resistance. It could be the viscosity of the blister fluid being forced through small pores or the viscosity of a film between the interdigitations of epidermis and dermis; viscous slip [2] could occur in fibrous bonds [3] or other structural elements in the junctional region; fibrous bonds connecting the two layers could remain intact themselves and be pulled out of a surrounding viscous medium.

In the interpretation of the viscous resistance as a fluid viscosity, examination of the influence of skin temperature offers a possibility for further investigation. For liquids, the higher the viscosity, the greater its dependence on temperature [4]. This dependence is illustrated in Figure 1 using data collected from various handbooks and tables. The progressive temperature dependence with increasing viscosity suggests that it would be informative to examine the influence of temperature on dermal-epidermal adherence. A strong influence of temperature would point to a high viscosity, a weak influence to a low viscosity.

Quantitatively, dermal-epidermal adherence (A) is determined as the product of suction pressure (p) and blistering time (t_b):

$$A = p\, t_b \qquad (1)$$

This implies that, if the suction pressure is kept the same, the influence of temperature on A may be found by examining the influence of temperature on t_b. In the theoretical models of dermal-epidermal adherence based on viscosity, the adherence (A) is directly proportional to the viscosity (η) [1]. Temperature has, therefore, the same relative influence on η as it has on A and, according to equation (1), also on t_b. In practice, the blistering time may be determined, for instance, at two temperatures 10° C apart. For that case the relations discussed read:

$$\eta_T/\eta_{(T+10)} = t_{b,T}/t_{b,(T+10)} \qquad (2)$$

It is possible to investigate the influence of temperature on the unknown viscosity involved in dermal-epidermal adherence by measuring the influence of temperature on blistering time. The results obtained in various stages, spaced over several years while experimental methods improved, are presented in this paper. Instigated by the observation of Evans and Naylor [5] that suction blisters form more easily on warm skin, Peachey also studied the influence of skin temperature on blistering time [6].

MATERIALS AND METHODS

Initially, we determined blistering times at two temperatures 10° C apart (see under b.). To reveal the type of relation between blistering time and skin temperature a more accurate method (described under a.) was developed which allows determinations of t_b over a wide range of temperatures.

(a) Blisters were elicited with an aluminum suction chamber as depicted in Figure 2. Skin temperature was measured with a copper-constantan thermocouple inside the chamber gently touching the skin area that was exposed to the suction pressure. Skin temperature was recorded throughout the experiments. Heating was achieved by means of an electric heating coil. The current through the coil was adjustable by hand. If cooling was

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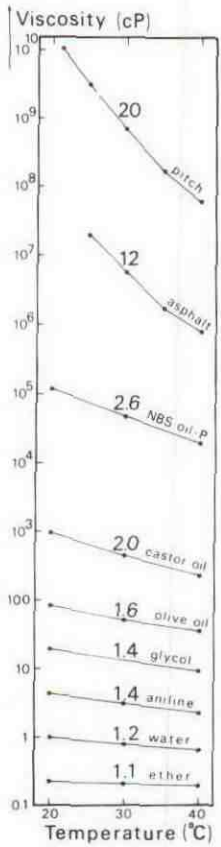

FIG. 1: The influence of temperature on the viscosity of several liquids. Viscosity is expressed in cP (centipoise; 1 cP = 0.001 N s m^{-2} [= 0.01 dyn s cm^{-2}]). The superimposed numbers represent the values of η_{24}/η_{34}, the ratio of the viscosities at 24° C and 34° C.

needed, cold water was pumped through a cooling circuit. This method allowed control of skin temperature within a few tenths of a degree C.

(b) Before these suction chambers became available, many data had already been gained from experiments carried out with a more circumstantial and less accurate method. The suction chambers were equipped only for measurement of the skin temperature. Heating was achieved with a hot-air jet, cooling with a spray refrigerant, both directed at the suction chamber. With this method suction experiments were performed at only 24° C and 34° C. Recordings of skin temperature showed variations of about 1.3° C during the experiments.

In all experiments the diameter of the suction orifice was 10 mm. Continuous inspection of the exposed skin was possible during the experiments. Blistering time was defined as the suction time needed to produce the first small blisters of about 0.5 to 1 mm in diameter.

RESULTS

Suction experiments were performed on the flexor side of the forearms of three male members of our department using method a. For each subject, blistering times were determined at a series of skin temperatures between 20° C and 43° C. Suction pressure was kept the same throughout a series of measurements. It was not equal for all subjects.

In Figure 3 the blistering times found are presented on a logarithmic scale. The straight lines are estimates of best fit. It appears that the relationship of blistering time and skin temperature is similar for all three subjects. Blistering time decreases rapidly and continuously over the entire range of temperatures studied.

The straight lines in Figure 3 indicate that blistering time is, approximately, an exponential function of temperature. The function may be described by the equation

$$t_b = C \exp(-BT) \qquad (3)$$

where C is a constant determined by the suction pressure and the adherence of the skin. The constant B characterizes the influence of temperature on the blistering time. A more practical figure serving the same purpose may be the ratio $t_{b,T}/t_{b,(T+10)}$ used in equation (2), which provides a Q_{10} of suction blister formation. Although the value of this ratio does not depend on the value of T that is used to calculate it, we take T = 24° C, where many data are available (see below). For three of the lines in Figure 3 the value of the ratio $t_{b,24}/t_{b,34}$ was calculated. The average of these values is approximately 4, which means that the blistering time at 24° C is about 4 times that at 34° C.

Suction experiments at skin temperatures 24° C and 34° C were performed on symmetrical skin fields on several subjects using method b. The averaged results obtained on abdomens of volunteers, on forearms of volunteers, and on abdomens of human cadavers are shown in the Table and are represented in Figure 3.

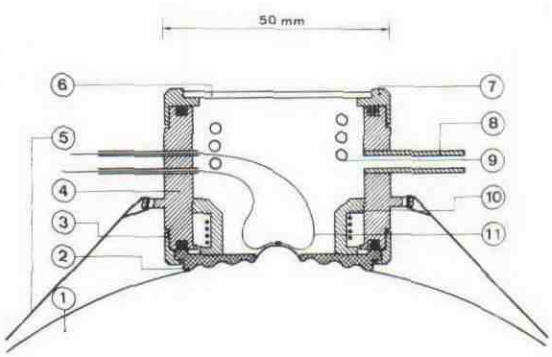

FIG. 2: Cross-section of a suction chamber on a subject's skin. 1, Skin; 2, interchangeable base-plate fixing the skin area to be exposed to suction; 3, ring for fixing base-plate to chamber; 4, wall of suction chamber; 5, elastic band to keep chamber in place; 6, glass window; 7, window setting; 8, plug to connect vacuum tube; 9, cooling circuit; 10, electric heating coil twisted around anodized aluminum ring which is connected to the chamber wall; 11, thermocouple measuring skin temperature.

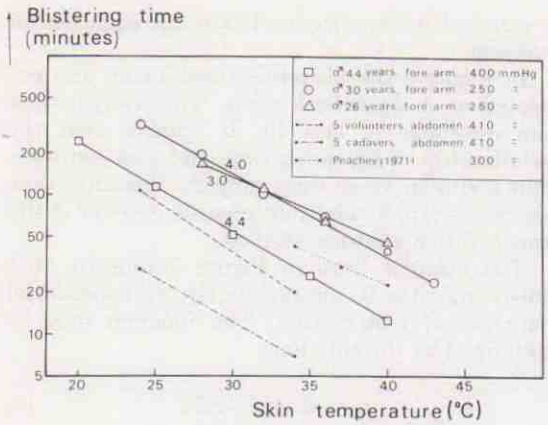

FIG. 3: The influence of skin temperature on blistering time plotted on a logarithmic scale. The values of $t_{b,24}/t_{b,34}$, the ratio of the blistering time at 24° C and 34° C, are superimposed.

DISCUSSION

The relationship of blistering time and skin temperature (Fig. 3) is of the same type as that of the viscosity of liquids and temperature (Fig. 1). Although this similarity is not in itself evidence of a viscous-like adherence, it gives additional support to the hypothesis of a dermal–epidermal bond based on viscosity proposed previously [1].

Quantitatively, the measurements obtained with accurate control of skin temperature (method a.) confirm those obtained with method b. in that a strong influence of temperature is found. The value $t_{b,24}/t_{b,34} \simeq 4$ is certainly more dependable than that found earlier ($t_{b,24}/t_{b,34} \simeq 5$), owing to the better control of temperature. Peachey [6] measured blistering times on 24 subjects at 34° C, 37° C, and 40° C. He also found a strong influence of temperature. From his results we determined for each temperature the mean of the 24 individual blistering times. These means are plotted in Figure 3 and seem to agree quite well with our results. Recently, Kiistala [7] also published data concerning the effect of skin temperature on suction blister formation in the range from 21° C to 39.4° C. The data agree with ours in that a strong influence of temperature is found; insofar as Kiistala's results on abdominal skin show an even stronger influence of temperature ($t_{b,T}/t_{b,(T+10)} \simeq 6.5$), it might be due to his rather improvised measurement of skin temperature.

In the interpretation of the various experimental findings in terms of a viscous bond, the strong influence of temperature points to a high viscosity. In principle, the viscosity of an unknown liquid may be estimated if the influence of temperature on the viscosity is known. This could be done by matching the temperature dependence of viscosity with the progression of slopes shown in Figure 1. The procedure is facilitated by Figure 4 where, for all liquids of Figure 1, the ratio η_{24}/η_{34} is plotted against the viscosity at 30° C (η_{30}) on a log-to-log scale. The temperature dependence of the dominating viscosity in the models of the adherence may be characterized by the ratio $\eta_{24}/\eta_{34} \simeq 4$, as follows from equation (2). Interpolation in Figure 4 reveals that $\eta_{24}/\eta_{34} \simeq 4$ corresponds to a viscosity at 30° C of about 10^5 cP. At a skin temperature of 35° C this will be reduced to 5×10^4 cP.

In one of the models of blister formation described earlier [1], the "inflow model," the formation of suction blisters is limited by the inflow of blister fluid. This fluid has a viscosity of only 2 cP, whereas we find an estimated value for the dominating viscosity of about 50,000 cP. Obviously, this result does not fit the inflow model. This negative conclusion with regard to the inflow model is in agreement with the evidence discussed previously [1]. In the other models of dermal–epidermal adherence that we proposed [1] the viscous bond is due either to some intermediary viscous substance or to the effect of viscous slip in filamentous material. A high viscosity value is to be expected in both cases; this is in better agreement with the strong influence of temperature. In fact, such models of the adherence are no more than possible examples; detailed location of the viscosity in the known structural elements of the junctional region is, so far, beyond the reach of our method.

It is questionable whether viscosity values up to 50,000 cP do occur in the region of the dermal–epidermal junction. Solutions of hyaluronic acid, a mucopolysaccharide probably present in the junctional region, may have viscosity values of 5,000 cP (at neutral pH) or even higher since the viscosity of such solutions varies enormously with changes in pH, ionic strength, and hyaluronic acid concentration [8]. Because little is known of the physico-

TABLE

Averaged results from suction experiments on healthy male volunteers and on human cadavers at skin temperatures 24° C and 34° C with suction pressure p = 410 mm Hg

Subjects	Site	Mean age	Number of subjects	Mean ± standard error of blistering time t_b in min		$t_{b,24}/t_{b,34}$
				24° C	34° C	
volunteers	abdomen	30	5	108 ± 18	20 ± 2	5.4 ± 1.0
volunteers	forearm	30	4	136 ± 20	29 ± 4	4.7 ± 0.9
cadavers	abdomen	71	5	39 ± 6	7 ± 1	5.6 ± 1.2

The experiments on cadavers were done within 18 hr of death and skin was stored at 0° C.

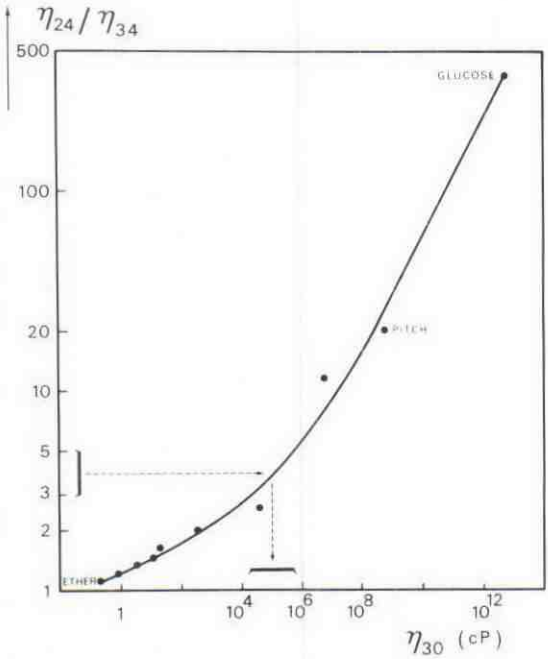

FIG. 4: Estimation of the viscosity involved in dermal–epidermal adherence derived from the data given in Figure 1. For all liquids in that figure, and for one additional substance with an even higher viscosity, the ratio of the viscosities at 24° C and 34° C against the viscosity at 30° C, both on logarithmic scales, have been plotted.

chemical state of hyaluronic acid in the junctional region, it is difficult to extrapolate from the available data to the viscosity values that may exist there.

The suggestion that dermal–epidermal separation by suction may depend on enzymatic action [6] is not very likely in view of the fact that practically all proteolytic enzymes have their optimal activity near 37° C, whereas blistering time tends to decrease with temperature at a constant slope up to 43° C (and even beyond 43° C as will be shown below); furthermore, below their optimal temperature most enzymatic reactions have relatively low Q_{10} values ($Q_{10} \simeq 1.5$). Heat-induced protein denaturation, which is another process readily thought of in relation to biologic effects of temperature, is known to have a Q_{10} in the order of 100; this process is, therefore, not attractive as an explanation of the influence of temperature on suction blister formation, where we found a Q_{10} of 4.

The marked influence of temperature on blistering time implies that skin temperature should be taken into account if various experimental results are to be compared. This is especially important with regard to comparison of measurements in vivo and in vitro. In excised skin at 0° C Kiistala [9] found an adherence as high as 25 times the value for normal skin. If corrected for the temperature difference, however, the value for excised skin comes out lower than the normal value.

The strong influence of temperature on dermal–epidermal adherence also has a few implications with respect to separation of epidermis and dermis as an experimental technique. A practical consequence is that, if separation is accomplished by suction, blistering time may be shortened appreciably by making the skin temperature as high as is acceptable in the context of the experiment. According to our experimental results, every increase of the skin temperature by 1° C lowers the blistering time by about 13 percent.

The findings reported also provide a plausible interpretation of a long-established technique for separating epidermis and dermis. Baumberger, Cowdry, and Suntzeff [10] found that, in excised skin, the epidermis could be easily removed from the dermis if the skin was heated to 50° C. The investigators also noticed that in skin so heated, the epidermis could no longer be removed with ease if they allowed the temperature to fall again. These findings of Baumberger et al have been interpreted as pointing to a reversible gel-sol transformation in a cementing substance between epidermis and dermis [11, 12]. However, the suction experiments described in our previous paper [1] suggest that even at normal skin temperature it is a sol state which dominates dermal–epidermal adherence, and in the continuous change of blistering time with temperature reported in the present paper there is no indication of any sudden transition of state between 20° and 43° C. If this change of blistering time with temperature would continue up to 50° C, it might well account for Baumberger's finding of easy separability at this temperature.

To check this possibility we performed a few experiments on abdominal skin obtained from autopsy. At a suction pressure of 250 mm Hg blistering times were 27 min at 30° C and 1.6 min at 50° C. The ratio $t_{b,30}/t_{b,50} = 17$ corresponds to a ratio $t_{b,T}/t_{b,(T+10)} = \sqrt{17} \simeq 4.1$. This value is in good agreement with our other observations. If the temperature of the abdominal skin is maintained at 50° C for some minutes (without external forces acting on it) and thereafter brought back to 30° C, the blistering time reaches a high value again—approximately 50 percent of the initial value at 30° C.

It is concluded that the relationship of blistering time and temperature found between 20° and 43° C indeed continues, in good approximation, up to 50° C. At 50° C this results in a blistering time so short that it clearly accounts for the ease with which epidermis and dermis can be separated at that temperature. In general, the variation of the viscosity of substances with temperature is reversible. Hence, Baumberger's observation that the adherence increases again if temperature is allowed to fall, is also accounted for by an interpretation of his findings in terms of the influence of temperature on viscosity.

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