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- (71) **Applicant** (*for all designated States except US*): **AVERY DENNISON CORPORATION** [US/US]; 150 N. Orange Grove Blvd., Pasadena, CA 91103 (US).
- (72) **Inventors; and**
- (75) **Inventors/Applicants** (*for US only*): **JOHNSON, Peter** [US/US]; 1000 Quiet Ridge Circle, Raleigh, NC 27614 (US). **WIBAUX, Anne, Marie** [FR/BE]; 22 Hof Ter Bekestraat, B-2018 Antwerpen (BE).
- (74) **Agents:** **BEMBENICK, Brian, G.** et al.; Avery Dennison Corporation, 8080 Norton Parkway, 22D, Mentor, OH 44060 (US).
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Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

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(54) **Title:** COMPREHENSIVE SKIN TESTING

(57) **Abstract:** Various methods and strategies are described for assisting and guiding the selection and formulation of an adhesive to be used by contacting skin. The methods are based upon correlations between various skin parameters and one or more physico-chemical properties of the adhesives.

COMPREHENSIVE SKIN TESTING

Cross-Reference to Related Applications

[0001] The present application claims priority upon US provisional patent application Serial No. 61/440,658 filed February 8, 2011.

Field of the Invention

[0002] The present invention relates to systems and methods for identifying one or more adhesives for use on a user's skin, based upon measurements of various parameters associated with the skin and/or a targeted location on the user's skin.

Background of the Invention

[0003] Various attempts are described in the prior art for assessing skin conditions. For example, US Patent 7,183,057 is directed to tape stripping methods for analysis of skin disease and pathological skin states. Specifically, the '057 patent describes non-invasive methods for detecting, monitoring, and diagnosing skin disease and pathological skin states such as irritated skin and psoriasis. The methods include using tape stripping to analyze expression in epidermal samples of one or more skin markers. In various examples of the '057 patent, the tape stripping is performed using pliable tape that has a rubber adhesive. Furthermore, the '057 patent describes methods for predicting and

monitoring response to therapy for a skin disease, such as psoriasis or dermatitis. Finally, the methods can include the use of a microarray.

[0004] In US Patent 5,015,431, a process is described for preparing model skin. Specifically, the '431 patent describes a process for making a model skin surface for testing adhesion of medical adhesive. Also described is a screening test which can be used as an alternative to costly and highly variable human skin substrates including casting silicone rubber on human skin to produce a mold having human skin topography and pouring a water-swellaable, water-soluble proteinaceous material along with a crosslinking agent and fatty acid constituent into the mold. The proteinaceous material crosslinks while in the mold and the water content of the material is adjustable to simulate varying moisture contents in human skin.

[0005] US Patent 6,687,621 is directed to methods for selecting polymers. That is, the '621 patent describes a predictive method for use in selecting or formulating polymers. The '621 patent describes a computational method for predicting a desired property and/or performance of polymers, and/or identifying and designing polymers that provide the noted desired property and/or performance. The desired property can be provided by the undiluted polymers, or diluted polymers in a composition.

[0006] US Patent Application Publication US 20070281314 is directed to methods for capturing and detection of micro-RNA molecules from the skin by non-invasive tape stripping. In this publication, non-invasive methods are described for isolating a miRNA molecule from an epidermal sample. Also described are methods of detecting, monitoring, and diagnosing skin disease and pathological skin states such as irritated skin and psoriasis. The methods include using tape stripping to obtain the miRNA from epidermal samples, and may be used to further analyze expression of one or more skin markers. In several examples of the '314 publication, the tape stripping is performed using pliable tape that has a rubber adhesive. Furthermore, the '314 publication describes methods for

predicting and monitoring response to therapy for a skin disease, such as psoriasis or dermatitis. Finally, the methods can include the use of a microarray.

[0007] Although satisfactory in many regards, none of the noted prior art provide methods for guidance in adhesive selection, and predicting safety and adhesive performance based upon correlations between the skin physiology and the physicochemical properties of the adhesive.

Summary of the Invention

[0008] The difficulties and drawbacks associated with previously known methods are addressed in the present method and system for correlating various skin parameters with physicochemical properties of adhesives, and using such correlations to efficiently and accurately guide formulation and/or selection of adhesives based upon specific user skin parameters.

[0009] In one aspect, the present invention provides a method for preparing correlations for guiding the selection of an adhesive for subsequent use along a user's skin. The method comprises measuring at least one skin parameter on a user's skin. The method also comprises preparing at least one set of adhesive samples in which the samples vary in a physicochemical property. The methods also comprise applying the at least one set of adhesive samples to the user's skin. The methods also comprise removing the adhesive samples from the user's skin. The methods also comprise measuring again, at least one skin parameter on the user's skin. And, the methods comprise correlating the physicochemical property of the adhesive samples with the at least one measured skin parameter.

[0010] In another aspect, the present invention provides a method for guiding the selection of an adhesive based upon at least one skin parameter of a user to which the adhesive is to be applied. The method comprises providing at least one correlation between one or more skin parameters of a user and one or more physicochemical properties of the adhesive. The method also comprises measuring at least one skin parameter on the user's skin. And, the method comprises applying the

measurements of the at least one skin parameter of the user's skin to the at least one correlation to thereby provide guidance as to the selection of the adhesive.

[0011] As will be realized, the invention is capable of other and different embodiments and its several details are capable of modifications in various respects, all without departing from the invention. Accordingly, the description is to be regarded as illustrative and not restrictive.

Detailed Description of the Embodiments

[0012] Adhesive performance on human skin primarily depends upon three groups of parameters: (i) physicochemical properties of the adhesive, mostly controlled by the base polymer and the adhesive formulation; (ii) interface between the human body and the adhesive, and specifically between the adhesive and the Stratum Corneum and skin physiology- topography, hydration, sebum secretion, trans epidermal water loss, skin movement, pH, etc.; and (iii) environment such as for example geographical area, physical activities, weather condition, etc. The latter group of parameters is difficult to measure and record, while in contrast, the first two groups of parameters can be controlled and/or measured.

[0013] A review of the literature concerning attempts to predict adhesive performance based on physicochemical parameters, reveals that while skin physiology is known to vary over an individual and between individuals, skin physiology has not been investigated as a parameter when trying to assess correlations between adhesion performance and physicochemical properties of the adhesives. A few studies from Molnlycke in collaboration with Cardiff University focused on correlating peel force at removal with trans epidermal water loss after adhesive removal and patient trauma at removal. Although those studies are useful in their approach to quantitatively evaluate pain and adhesive performances, they do not provide any guidance as to skin physiology parameters and optimal adhesives for adhesive tape or other application.

[0014] While tape stripping is an established procedure in Stratum Corneum (SC) physiology research, dermatology and transdermal drug delivery, it is not commonly used for adhesive development. Interestingly, there are similarities in applying and removing adhesive tape onto a human body and SC stripping in that when removing medical adhesive from human body, SC stripping occurs as one of the major disadvantages. Different factors are known to affect the outcome of the barrier damage and amount of Stratum Corneum removed with tape stripping. Such factors are: anatomical site, temperature, time of the day, intensity and duration of the applied pressure, sex, age, skin furrow, and material and tape used. Those factors are identical to those influencing adhesion of medical adhesives to human skin.

[0015] In view of these and other observations, it was concluded that investigating skin physiology before and after adhesive application, as well as using Stratum Corneum remaining on removed dressing/adhesive could provide valuable information and guidance in the selections and development of adhesives.

[0016] The adhesive selection methods are appropriate to characterize the skin and adhesive interface before and after adhesive application. The various methods described herein include non-invasive test methods as well as practical methods that can be readily performed in a laboratory.

[0017] After reviewing the fields of dermatology, Stratum Corneum physiology research, and transdermal drug delivery, it was concluded that combining skin studies before application of the tape with wear performance will provide helpful insight and understanding adhesive properties required depending on skin type and/or body area. Assessing skin after removal of the dressing will also provide guidance and a better understanding of product safety and generate useful marketing data on products.

[0018] The present invention is based upon a discovery that selection of an adhesive for use on a user's skin can be performed or at least significantly promoted by using one or more correlations between various skin physiologic parameters and physicochemical properties of adhesives.

Specifically, correlating one or more skin physiologic parameters such as (i) biometric parameters and/or (ii) biological markers carried in the adhesive after removal from the user's skin, with the physicochemical properties of the adhesives of interest, can predict wear performances and adhesive safety.

[0019] The skin parameters which can be correlated include biometric parameters such as but not limited to skin hydration, trans epidermal water loss, skin surface pH, skin color, sebum, skin topography, skin thickness, and combinations of these parameters.

[0020] The skin parameters may also include biological markers which typically relate to the Stratum Corneum, and are typically located in the adhesive upon removal of the article adhered to the user by the adhesive. Non-limiting examples of such biological markers include but not limited to inflammation markers (IL-8, IL1-Ra, IL1alpha), nucleic acid based markers (RNA, DNA), sebum composition, proteins, and combinations thereof. Generally, the biological marker can be any biological compound which is measurable, and which originates from the Stratum Corneum.

[0021] Examples of the physicochemical properties of the adhesive polymer include but are not limited to glass transition temperature (Tg), molecular weight, and polarity.

[0022] A representative strategy in accordance with the present invention for guiding adhesive selection is as follows. Various skin parameter measurements are obtained from an individual, a set or group of individuals, and/or at certain designated areas on a user's (or users') body. These measurements of skin parameters can for example, include measurements of skin hydration, trans epidermal water loss, skin surface pH, skin color, sebum, skin topography, skin thickness, and the like. In another operation, a series of samples of the adhesive are prepared. The series of samples vary in terms of one or more physicochemical properties of the adhesive polymer, such as glass transition temperature (Tg), molecular weight, polarity, and the like. Thus for example, one series of adhesive samples may include 10 samples in which the adhesive base polymer used in each sample exhibited a

different molecular weight. It will be appreciated that other series of adhesive samples can be prepared in which the samples vary by glass transition temperature (T_g), or by polarity, or by some other characteristic. The various adhesive samples are then applied to the user's skin and preferably to the same location on the skin at which the previously noted measurements of skin parameters were obtained. Typically, the various adhesives will be left on the user or users for a period of time that is representative of the intended use of the adhesive. For example, if the evaluation is with regard to adhesives for wound dressings, the samples are preferably left on the user(s) for at least several hours, and more preferably for a day or more. After a sufficient time period has passed, the adhesive samples are removed from the user(s). In one aspect of the invention, one or more skin parameters such as biometric parameters are then measured along the user's skin and preferably at the same location at which the adhesive was contacting. In another aspect of the invention, skin parameters such as biological markers carried in the adhesive after removal from the user's skin, are analyzed. Correlations are then prepared by comparing each set of samples with one or more set of measurements of skin parameter(s). For example, comparing or plotting a set of skin parameter measurements with a set of adhesive samples that vary by molecular weight of the base adhesive polymer, may reveal what molecular weights or range of molecular weights are best to use to minimize loss of skin hydration. Another example involves comparing or plotting a set of skin parameter measurements with a set of adhesive samples that vary by glass transition temperature of the adhesive base polymer. Such a correlation would likely reveal the best T_g's to use in an adhesive formulation to improve or optimize one or more skin parameters. In addition, the invention includes the use of correlating one or more physicochemical properties of the adhesives with both types of skin parameters, e.g. the (i) biometric parameters and/or (ii) biological markers carried in the adhesive after removal from the user's skin.

[0023] It is also contemplated that the present invention can be readily applied to the analysis of any stripped tissue components and specifically, includes metabolomic and histologic

assessment to the RNA and DNA analyses. This allows detection of pathways of metabolic response to early sensitivity, for example.

[0024] In certain applications, the methods described herein can involve application of adhesive samples to multiple sites or locations on a user's (or users') body simultaneously. The relative performance of the adhesive samples applied at different locations is then assessed. This strategy enables a practitioner to review "behavior rations" based upon differences in skin mobility, dryness, oiliness, etc.

[0025] Many other benefits will no doubt become apparent from future application and development of this technology.

[0026] All patents, published applications, and articles noted herein are hereby incorporated by reference in their entirety.

[0027] As described hereinabove, the present invention solves many problems associated with previously known practices. However, it will be appreciated that various changes in the details, materials and arrangements of components and/or operations, which have been herein described and illustrated in order to explain the nature of the invention, may be made by those skilled in the art without departing from the principle and scope of the invention, as expressed in the appended claims.

Claims

What is claimed is:

1. A method for preparing correlations for guiding the selection of an adhesive for subsequent use along a user's skin, the method comprising:

measuring at least one skin parameter on a user's skin;

preparing at least one set of adhesive samples in which the samples vary in a physicochemical property;

applying the at least one set of adhesive samples to the user's skin;

removing the adhesive samples from the user's skin;

measuring again, at least one skin parameter on the user's skin; and

correlating the physicochemical property of the adhesive samples with the at least one measured skin parameter.

2. The method of claim 1 wherein the at least one skin parameter is selected from the group consisting of (i) biometric parameters, (ii) biological markers carried in the adhesive after removal from the user's skin, and (iii) combinations of (i) and (ii).

3. The method of claim 2 wherein the at least one skin parameter is a biometric parameter.

4. The method of claim 3 wherein the biometric parameter is selected from the group consisting of skin hydration, trans epidermal water loss, skin surface pH, skin color, sebum, skin topography, skin thickness, and combinations of these parameters.

5. The method of claim 2 wherein the at least one skin parameter is a biological marker.

6. The method of claim 5 wherein the biological marker is selected from the group consisting of inflammation markers (IL-8, IL1-Ra, IL1alpha), nucleic acid based markers (RNA, DNA), sebum composition, proteins, and combinations thereof.

7. The method of any one of claims 1-6 wherein the physicochemical property of the adhesive is selected from the group consisting of glass transition temperature (Tg), molecular weight, and polarity.

8. A method for guiding the selection of an adhesive based upon at least one skin parameter of a user to which the adhesive is to be applied, the method comprising:

providing at least one correlation between one or more skin parameters of a user and one or more physicochemical properties of the adhesive;

measuring at least one skin parameter on the user's skin; and

applying the measurements of the at least one skin parameter of the user's skin to the at least one correlation to thereby provide guidance as to the selection of the adhesive.

9. The method of claim 8 wherein the one or more skin parameters is selected from the group consisting of (i) biometric parameters, (ii) biological markers carried in the adhesive after removal from the user's skin, and (iii) combinations of (i) and (ii).

10. The method of claim 9 wherein the at least one skin parameter is a biometric parameter.

11. The method of claim 10 wherein the biometric parameter is selected from the group consisting of skin hydration, trans epidermal water loss, skin surface pH, skin color, sebum, skin topography, skin thickness, and combinations thereof.

12. The method of claim 9 wherein the at least one skin parameter is a biological marker.

13. The method of claim 12 wherein the biological marker is selected from the group consisting of inflammation markers (IL-8, IL1-Ra, IL1alpha), nucleic acid based markers (RNA, DNA), sebum compositions, proteins, and combinations thereof.

14. The method of any one of claims 8-13 wherein the physicochemical property of the adhesive is selected from the group consisting of glass transition temperature (T_g), molecular weight, and polarity.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/024277

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/103 A61L15/58
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 611 575 A1 (JOHNSON & JOHNSON CONSUMER [US]) 24 August 1994 (1994-08-24) page 2, line 1 - line 4 page 3, line 12 - line 22 page 3, line 40 - line 42 page 4, line 1 - page 5, line 38 tables 1,2 figures 1-3	1,8
A	US 5 876 855 A (WONG ROY [US] ET AL) 2 March 1999 (1999-03-02) column 1, line 30 - line 48 column 2, line 50 - column 3, line 48 column 10, line 47 - line 67 ----- -/--	1,8

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Völlinger, Martin

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/024277

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Information on patent family members

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