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(71) Applicant (for all designated States except US): **HOLLISTER INCORPORATED** [US/US]; 2000 Hollister Drive, Libertyville, Illinois 60048 (US).

(72) Inventors; and

(71) Applicants (for US only): **TAYLOR, Michael** [US/US]; 611 Ambria Drive, Mundelein, Illinois 60060 (US).
MURAHATA, Richard [US/US]; 2360 W. Steeple Chase Circle, Libertyville, Illinois 60048 (US).

(74) Agent: **VANDERLEEDEN, Kevin**; McCormick, Paulding & Huber LLP, CityPlace II, 185 Asylum Street, 18th Floor, Hartford, Connecticut 06103 (US).

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(54) Title: BUFFERED ADHESIVE COMPOSITIONS FOR SKIN-ADHERING PRODUCTS AND METHODS OF MAKING SAME

(57) Abstract: Buffered adhesive compositions comprising a high molecular weight polymeric buffer and products such as wound dressings and ostomy skin barriers incorporating the compositions. Use of high molecular weight polymers that are rich in acidic sites. Polymers with polyacid unctonality can serve as buffers through the use of mixtures of their protonated and neutralized forms. A wound dressing that includes a flexible outer layer and a high molecular weight polymeric buffering adhesive applied to one side thereof, said adhesive providing pH buffering and fluid absorption with minimal irritation to a wearer's skin. An ostomy skin barrier that includes a high molecular weight polymeric buffering adhesive applied to one side thereof, said adhesive composition providing pH buffering and fluid absorption with minimal irritation to a wearer's skin.



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**BUFFERED ADHESIVE COMPOSITIONS FOR SKIN-ADHERING
PRODUCTS AND METHODS OF MAKING SAME**

CROSS-REFERENCE TO RELATED APPLICATIONS

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This application claims priority from United States provisional applications 61/604,663, filed February 29, 2012, and 61/668,178, filed July 5, 2012, each of which is incorporated herein by reference in its entirety.

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FIELD OF THE DISCLOSURE

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This disclosure relates to the technical field of adhesive compositions for medical dressings and skin-adhering devices such as ostomy products, wound dressings, and other medical products intended to be adhesively secured to skin surfaces of users. The disclosure is specifically concerned with such adhesive compositions that contain a high molecular weight buffer and are capable of absorbing fluids and maintaining normal skin pH levels and to methods for making the compositions.

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BACKGROUND

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In a number of medical uses, a product is adhered directly to the skin, such as in the case of a wound dressing or an ostomy skin barrier. Such a product must be securely affixed to the skin to keep it in place and must absorb whatever fluid is produced under or near it, such as perspiration, wound exudate, fluid fecal matter, and the like.

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Wound dressings typically perform several functions to facilitate healing. These functions include absorbing wound exudate, regulating pH to create an optimal healing environment and reduce microbial activity, and protecting the wound from infection. Many such wound dressings are self-adhesive and contain an adhesive layer that typically adheres to the peri-wound skin of a wearer. It is known that skin often becomes irritated under wound dressings.

Known wound dressings achieve the aforementioned functionality through the use of several individual components. For example, known dressings often use

hydrocolloids, e.g., carboxymethylcellulose (CMC), pectin, or gelatin, to absorb wound exudate. While some hydrocolloids are also capable of independently adjusting pH, the degree of pH buffering they can provide is limited by the amount of available hydrocolloid in the dressing, which, in turn, is dependent on the desired fluid handling properties of the dressing. Moreover, the buffering effect of hydrocolloids alone is not optimal.

Moreover, the manufacture of adhesive compositions containing hydrocolloids such as those described above requires multiple steps, due to the temperature-sensitivity of these materials. It would be preferred to minimize the number of preparative steps (ideally to just one) and the number of separate ingredients.

Adhesive compositions containing hydrocolloids are well known, as disclosed, for example, in U.S. Pat. Nos. 5,571,080, 3,339,546, 4,192,785, 4,296,745, 4,367,732, 4,813,942, 4,231,369, 4,551,490, 4,296,745, 4,793,337, 4,738,257, 4,867,748, 5,059,169, and 7,767,291, the disclosures of which are incorporated herein by reference. Hydrocolloids are commonly used in what is commonly referred to as hydrocolloid skin barriers or hydrocolloid wound dressings. Such skin barriers and wound dressings normally include a water-insoluble pressure-sensitive adhesive as a continuous phase with particles of one or more hydrocolloids dispersed throughout the adhesive as a liquid-absorbing and swellable discontinuous phase.

The water-insoluble adhesive phase of commercial skin barriers and wound dressings typically consists of polyisobutylene (PIB), or block copolymers such as styrene-isoprene-styrene (SIS), or blends of these materials. The surface tack may be modified by the addition of tackifier components.

Patients with a permanent or temporary ostomy (colostomy, ileostomy, and the like) have need of a pouch to contain the expelled fecal material or urine. The pouch is normally attached to the peristomal skin with an adhesive skin barrier that attaches the pouch to the skin. A skin barrier is normally replaced every three to five days but may remain in place for up to a week. During use of the barrier, the peristomal skin may become irritated due to prolonged contact with the fecal material. Over time, the irritation can become severe.

In some applications, an ostomy skin barrier has an adhesive tape border around its periphery for additional security. The adhesive for said border is typically an acrylic

adhesive. As used herein, the term “skin barrier” is intended to include any skin barrier either with or without an adhesive tape border.

Both wound exudate and fecal material contain proteolytic and lipolytic enzymes. These enzymes, when contained in a closed, moist environment, are thought to degrade the stratum corneum and contribute to the observed irritation. Moreover, since both wound dressings and ostomy skin barriers are normally removed and re-applied on a regular basis, the integrity of the skin under them becomes compromised and more susceptible to irritation than normal skin.

Normal skin has a so-called “acid mantle” which maintains the surface of the skin at a pH typically between about 4.0 and 5.5 (slightly acidic). This pH range promotes the growth of beneficial microorganisms and retards the growth of harmful microorganisms, while helping to maintain the integrity of the skin. At this pH level, the activity of (and hence the damage caused by) the proteolytic and lipolytic enzymes from wound exudate or fecal matter would not be severe. However, the wound exudate and stomal fluid normally have a pH in the range of 6.0 to 8.0. This increase in pH causes a significant increase in the activity of the enzymes and hence in their ability to cause irritation.

Current skin barriers incorporating hydrocolloids such as pectin and CMC do have limited pH buffering capacity. When exposed to water or saline solution, they are capable of adjusting pH to a level in the desired range from about 4.0 to 5.5. However, it is important to note that physiological fluids such as stoma output or wound exudates are buffered, typically at pH levels close to neutral. When current skin barriers are exposed to such fluids, the buffering capacity inherent in the physiological fluid overwhelms the weak buffering capacity of the skin barrier. As a result, the pH at the surface of the skin barrier increases to approach the pH of the fluid used to challenge the skin barrier. Thus, it is desirable to provide a skin barrier with enhanced pH buffering capacity.

In view of the above, it would be desirable to have an adhesive composition containing a suitable buffer to maintain the pH of the skin under a wound dressing or a stomal skin barrier or the like product at about 4.0 to about 5.5 without being inherently irritating to the user's skin. It would also be desirable to have such a composition that could be manufactured in a minimal number of steps and using a minimal number of ingredients.

SUMMARY

In accordance with one aspect of the disclosure, a high molecular weight polymeric buffering adhesive is provided that is capable of fluid absorption and pH buffering.

In accordance with another aspect of the disclosure, a method is provided for preparing the high molecular weight polymeric buffering adhesive.

In accordance with another aspect of the disclosure, a wound dressing is provided that includes a high molecular weight polymeric buffer capable of fluid absorption and pH buffering.

In accordance with another aspect of the disclosure, an ostomy skin barrier is provided that includes a high molecular weight polymeric buffer capable of fluid absorption and pH buffering.

In accordance with another aspect of the disclosure, a method is provided for using the high molecular weight polymeric buffer to manufacture a skin-adhering device such as a skin-adhering medical device.

An embodiment of the disclosure is a wound dressing that includes a flexible outer layer and a high molecular weight polymeric buffering adhesive applied to one side thereof, said adhesive providing pH buffering and fluid absorption with minimal irritation to a wearer's skin.

Another embodiment of the disclosure is an ostomy skin barrier that includes a high molecular weight polymeric buffering adhesive applied to one side thereof, said adhesive composition providing pH buffering and fluid absorption with minimal irritation to a wearer's skin.

DESCRIPTION OF A PREFERRED EMBODIMENT

One embodiment of the present disclosure is directed to an adhesive composition comprising a high molecular weight buffer that absorbs fluids such as perspiration, wound exudate, and fecal matter, adjusts pH, and reduces enzymatic activity.

In particular, an embodiment of the present disclosure contemplates use of high molecular weight polymers that are rich in acidic sites. Polymers with polyacid

functionality can serve as buffers through the use of mixtures of their protonated and neutralized forms. Indeed, the abundance of acidic sites enables a single polymer to be partially neutralized so that each polymer chain has both acidic and basic sites, thereby forming an effective buffer from a single polymer species. Any high molecular weight polymer having pendant carboxyl groups that are capable of being partially neutralized is suitable for use in the present disclosure. Suitable polymers include, for example, polyacrylic acid and poly(2-alkyl acrylic acid) in which the alkyl chain is from one to five carbons in length and may be straight chain or branched chain. Poly methacrylic acid is the preferred poly (2-alkyl acrylic acid). Other suitable polymers are copolymers of any of acrylic acid and 2-alkyl acrylic acid monomers, copolymers of the foregoing monomers with maleic acid, olefinic polymers substituted with side chains containing free carboxylic acid groups, such as polyvinyl alcohol esterified with a diacid, triacid or polyacid (e.g., polyvinyl alcohol succinate), and the like. As will be appreciated by one of skill in the relevant art, the buffering adhesive composition of the disclosure can employ any high molecular weight polymer having partially neutralizable pendant carboxyl groups that is capable of maintaining the pH of a test product at less than about 6.0 in the phosphate buffer challenge test described in Example 1.

Polymers particularly well suited for use in an embodiment of the disclosure include polyacrylic acid (PAA) and polymethacrylic acid (PMA). Both PAA and PMA are available from, for example, Sigma-Aldrich Co., in a variety of forms, e.g., powder and solution, and in a range of molecular weights. Of the acrylic acid derivatives, PAA is preferred because it has the highest density of carboxylic acid sites per gram of compound and hence the highest extent of buffering per gram of compound. As used herein, "high molecular weight" PAA means greater than about 60,000 Daltons and as high as several million Daltons. The term has similar meanings for PMA and the other polymers described above.

As discussed above, these poly-acidic polymers can be partially neutralized to provide both the acid and salt components of the buffer system on the same molecule. Typical extents of neutralization are from about 20% to about 40%, preferably from about 25% to about 37% for PAA and similar values for other polymers. These ranges include all values within the end points, and particularly 28%, 31%, 34%, and 36%. One of ordinary skill in the art can readily determine the appropriate degree of neutralization for a particular polymer and use, particularly to achieve the desired pH

buffering range. Partial neutralization of PAA may be achieved by mixing PAA (plus water if appropriate) with a stoichiometrically appropriate amount of a strong base (e.g., NaOH) until the desired degree of neutralization is achieved. Other polymers may be treated similarly. Partially neutralized polyacids such as PAA are also available commercially.

PAA and related polymers exist in both cross-linked and non cross-linked forms and the degree of cross-linking can be varied. Cross-linked PAA is known to be an excellent absorbent. The polymers used in the present disclosure, however, are preferably not cross-linked. The inventors have discovered that cross-linked PAA (for example) may be excessively absorbent, and its use in the present disclosure would lead to excessive swelling and possible rupture of the product in which it is being used. Moreover, non cross-linked PAA and related polymers are preferred because of their ability to form mucoadhesives to aid in the retention on the skin of the device with which the adhesive composition of the disclosure is used.

As stated, high molecular weight polymers, e.g., PAA and PMA, both provide effective pH buffering and absorb fluids such as perspiration, wound exudate, or fecal matter. More specifically, the polymers function similarly to hydrocolloids such as pectin and CMC when dispersed within an adhesive matrix. That is, they absorb and swell and form viscous solutions that provide mucoadhesion against a wearer's skin. As will be appreciated, the high molecular weight polymers may be the sole hydrocolloid component or in other embodiments, they may be combined with other hydrocolloids, depending on the application and desired fluid handling capabilities of the wound dressing or skin barrier.

In one embodiment of the disclosure, high molecular weight PAA is combined with polyisobutylene and either styrene-isoprene-styrene copolymer or polymer fibers (or both) for increased strength. In one such embodiment, the adhesive composition comprises high molecular weight PAA, polyisobutylene, and styrene-isoprene copolymer. In another such embodiment, the adhesive composition comprises high molecular weight PAA, polyisobutylene, styrene-isoprene copolymer and fibers such as cotton or preferably polyolefin such as polyethylene or polypropylene.

The adhesive component of the compositions of this disclosure may be any material that has pressure-sensitive adhesive properties with a strong affinity for the material of the fibers. It may be a single pressure-sensitive adhesive or a combination of

two or more pressure-sensitive adhesives. Adhesives useful in the present disclosure include, for example, those based on natural rubbers, synthetic rubbers, styrene block copolymers, polyvinyl ethers, poly(meth) acrylates (including both acrylates and methacrylates), polyolefins and silicones. A particular adhesive believed to be a preferred material of choice for this disclosure is a polyolefin, namely, polyisobutylene (PIB), but other pressure-sensitive adhesive materials having similar properties are believed suitable.

The fibers in the adhesive composition may be any fibrous material known in the art but preferably are compatible with, and even have a strong affinity for, the tacky adhesive component. It has been found that polyolefins such as polyethylene and polypropylene are highly compatible with PIB and are easily wetted by that adhesive medium. Both are non-polar saturated hydrocarbons.

In one embodiment of the manufacture of the adhesive composition, a high molecular weight polymeric buffering adhesive such as PAA or PMA and a pressure-sensitive adhesive such as PIB are combined in a single mixing step. Other materials such as SIS and/or polypropylene fibers may additionally be combined in the single mixing step. This manufacturing embodiment has the benefit of avoiding multiple mixing steps, thereby saving time and minimizing equipment use. A preferred embodiment in this manufacture is the combination of the desired amounts of PAA, PIB, and SIS in a single mixing step.

Preferably such PIB is present as relatively high molecular weight PIB (molecular weight in the range of about 40,000 to 60,000). For example, a skin barrier for ostomy use would normally contain 60,000 molecular weight PIB in the range of 50 wt.% to 65 wt.% or 40,000 molecular weight PIB in the range of 40 wt. % to about 55 wt. %.

Additionally, combinations of 40,000 molecular weight and 60,000 molecular weight PIB may also be used, such as 32.5 wt.% 40,000 molecular weight PIB and 32.5 wt.% 60,000 molecular weight PIB.

Preferably, the partially neutralized high molecular weight polyacid (e.g., PAA) comprises from about 20 wt.% to about 45 wt.% of the adhesive composition. The PIB component may comprise from about 40 wt.% to about 65 wt.% of the adhesive composition. The SIS component may comprise from about 0 wt.% to about 25 wt.% of the adhesive composition. Preferably, the adhesive composition comprises from about 20 wt.% to about 45 wt.% partially neutralized polyacrylic acid, from about 40 wt. % to

about 55 wt.% PIB, and from about 5 wt.% to about 15wt.% SIS. One preferred adhesive composition comprises about 45 wt.% partially neutralized PAA, about 40 wt.% PIB, and about 15 wt.% SIS. Another preferred adhesive composition comprises about 30 wt.% partially neutralized PAA, about 55 wt.% PIB, and about 15 wt.% SIS. Another preferred adhesive composition comprises about 54 wt.% PIB, about 6 wt.% polyethylene fibers, and about 40 wt.% 25% neutralized high molecular weight PAA. Still another preferred adhesive composition comprises about 51 wt.% PIB, about 20 wt.% SIS, about 2 wt.% polyethylene fibers, and about 27 wt.% 35% neutralized high molecular weight PAA. In the latter two compositions, the PIB is preferably Nippon Himol 4H as described below.

Whatever materials are chosen for the buffering adhesive composition of the disclosure, it is highly desirable that the composition be at least minimally absorptive. The buffering capability of the present compositions is related in part to their absorptive capability. If no absorption were to occur, the high molecular weight polymeric buffer would not be contacted by the wound exudate or fecal material and hence would not be effective. Although compositions having lower absorptive capacity are included within the present disclosure, the compositions of the disclosure should preferable have an absorptive capacity of at least about 0.15 g/cm² as measured in the test of Example 1. The buffering capability of compositions having lower absorptive capacity is less optimal.

The following Examples describe the manufacture and testing of representative embodiments of the disclosure.

Example 1:

Test Samples: Test samples were prepared by heat compression of barrier materials to a thickness of 0.020 inches and were laminated between a removable release liner and a flexible backing film.

Materials

Polyisobutylene (PIB)

Oppanol® B10 with viscosity average molecular weight 40,000 produced by BASF
Oppanol® B12 with viscosity average molecular weight 55,000 produced by BASF

Nippon Himol 6H with viscosity average molecular weight 60,000 produced by JX Nippon Oil and Energy

Nippon Himol 4H with viscosity average molecular weight 40,000 produced by JX Nippon Oil and Energy

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Styrene-Isoprene-Styrene block copolymer (SIS)

Kraton™ D-1161P produced by Kraton Polymers

Polyolefin Fibers

10 Polyethylene Short Stuff Synthetic Pulp E380F supplied by MiniFIBERS, Inc.

Polypropylene Short Stuff Synthetic Pulp Y600F supplied by MiniFIBERS, Inc.

Polyacrylic Acid aqueous solutions

Noverite™ K-702 25% aqueous solution with molecular weight 345,000 produced by

15 Lubrizol

ACUMER™ 1510 25% aqueous solution with molecular weight 60,000 produced by Dow

Partially neutralized Polyacrylic Acid

20 Polyacrylic acid in water was neutralized to the desired degree by addition of aqueous sodium hydroxide. The resulting solution of partially neutralized polyacrylic acid was dried in aluminum trays at 150°C for approximately 20 hours. The dried material was crushed and then ground in a hammer mill (Model JT, Homiloid Machine, Fitzpatrick Corporation). Laser light scattering particle size analysis of different batches showed
25 mean particle sizes in the range from 70 to 150 microns.

In addition, partially neutralized Polyacrylic Acid was obtained pre-neutralized in dry powder form:

Aronvis AH-106X (35% neutralized Polyacrylic acid) produced by Toa Gosei.

30 **Fluid Absorption and pH:** Fluid absorption was measured following the practice of standard EN 13726-1:2002 (Test methods for primary wound dressings – Part 1: Aspects of absorbency, Section 3.3). The hydrating fluid was normal saline (0.9% NaCl in water). The mass of fluid absorbed was measured by the weight gain in samples of 10

cm² surface area exposed to 20 mL normal saline. Samples were maintained in an oven (37°C, 15% relative humidity) for fixed time periods. Surface pH measurements were performed on samples following fluid absorption using a calibrated pH meter and a flat pH probe (Ross® model 8135BN).

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pH Buffer Challenge: A stock buffer solution (100 mM in Phosphate, 0.9% NaCl, pH 7.4) was prepared. Lower phosphate concentration buffers were prepared by dilution of the stock buffer with appropriate volumes of 0.9% NaCl. A 10 cm² surface of the barrier was exposed to 10 mL of buffer challenge solution.

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A series of formulations based on PIB, polyethylene fibers and partially neutralized polyacrylic acid (with two different molecular weights and two different degrees of neutralization) were prepared.

15 Example 2:

Compositions were prepared using a Brabender Type REE6 mixer at 85°C. The required amounts of polyethylene fibers and partially neutralized polyacrylic acid were pre-blended. The required weight of PIB was added to the mixer and was mixed at 36 rpm for 2 minutes. The pre-blended fibers and powder were added over the course of 3
20 minutes while mixing at 36 rpm. The mixing chamber was sealed and vacuum was applied and mixing was continued for 15 minutes. Vacuum was released and the mixtures were removed from the mixer and allowed to equilibrate at room conditions before any testing was undertaken. Table 1 below shows compositions prepared in this fashion with weight percentages of the indicated ingredients along with testing results
25 for these compositions. In Table 1 and Table 2 below, the 6 Hour and 24 Hour Buffer Challenges used a 100 mM phosphate buffer at pH 7.4 in 0.9% NaCl solution.

Table 1

Polyisobutylene Openet 912	Polyethylene fiber	Polyacrylate Buffer	Polyacrylic acid source	Percent Neutralized	6 Hour Fluid Absorption g/cm ²	6 Hour Surface pH	24 Hour Fluid Absorption g/cm ²	24 Hour Surface pH	6 Hour Buffer Challenge Surface pH	24 Hour Buffer Challenge Surface pH
65.0%	4.0%	31.0%	ACUMER™ 1510	37.5	0.015	4.82	0.019	4.97	7.29	7.00
51.0%	4.0%	45.0%	ACUMER™ 1510	25	0.184	4.26	0.425	4.17	5.10	4.99
52.8%	6.3%	41.1%	Noverite™ K-702	25	0.209	4.15	0.524	4.11	5.39	5.32
48.5%	8.5%	45.0%	ACUMER™ 1510	37.5	0.057	4.74	0.219	4.88	6.28	5.53
55.0%	5.0%	30.0%	ACUMER™ 1510	25	0.033	4.39	0.123	4.22	6.55	5.91
47.0%	8.0%	45.0%	ACUMER™ 1510	37.5	0.034	4.75	0.061	4.72	6.56	5.48
51.9%	8.0%	40.1%	ACUMER™ 1510	25	0.084	4.28	0.247	4.21	5.89	5.21
62.0%	8.0%	30.0%	ACUMER™ 1510	25	0.031	4.39	0.047	4.38	6.79	6.05
47.0%	8.0%	45.0%	Noverite™ K-702	25	0.222	4.34	0.576	4.43	5.37	5.10
65.0%	4.0%	31.0%	ACUMER™ 1510	25	0.074	4.23	0.200	4.23	6.38	5.32
55.0%	4.0%	31.0%	Noverite™ K-702	25	0.123	4.44	0.306	4.45	5.98	5.53
47.0%	8.0%	45.0%	Noverite™ K-702	37.5	0.170	4.81	0.468	4.57	5.71	5.67
62.0%	8.0%	30.0%	Noverite™ K-702	25	0.057	4.51	0.246	4.83	6.91	5.78
58.5%	4.0%	37.4%	ACUMER™ 1510	37.5	0.030	4.73	0.085	4.82	6.96	6.24
51.0%	4.0%	45.0%	Noverite™ K-702	37.5	0.237	4.81	0.559	4.88	5.62	5.55
53.8%	8.0%	38.2%	Noverite™ K-702	37.5	0.076	5.05	0.316	4.93	6.54	5.76
62.0%	8.0%	30.0%	Noverite™ K-702	37.5	0.030	5.22	0.040	5.01	7.28	7.08
62.0%	8.0%	30.0%	ACUMER™ 1510	37.5	0.031	4.81	0.029	4.51	7.40	7.24
51.0%	4.0%	45.0%	Noverite™ K-702	25	0.299	4.42	0.616	4.38	5.31	5.37
47.0%	8.0%	45.0%	ACUMER™ 1510	25	0.183	4.21	0.365	4.20	5.83	5.67
65.0%	5.0%	30.0%	Noverite™ K-702	37.5	0.027	5.03	0.068	5.02	7.19	6.47
62.0%	8.0%	30.0%	ACUMER™ 1510	37.5	0.028	4.75	0.029	4.76	7.32	7.16
51.0%	4.0%	45.0%	ACUMER™ 1510	37.5	0.107	4.74	0.214	4.72	6.45	5.33
65.0%	4.0%	31.0%	Noverite™ K-702	37.5	0.062	4.89	0.168	4.82	7.01	5.96

5 Example 3:

A second series of formulations based on PIB (two different molecular weights), Styrene-Isoprene-Styrene copolymer and partially neutralized polyacrylic acid (25% neutralized Noverite K-702) were prepared.

Compositions were prepared using a Brabender Type REE6 mixer at 140°C. The required weight of SIS was added to the mixer and was mixed at 36 rpm for 7 minutes. The required amount of PIB and mixing was continued at 36 rpm. The mixer speed was increased to 100 rpm and mixing was continued for another 11 minutes. The required amount of partially neutralized polyacrylic acid (25% degree of neutralization) was added and mixing was continued for 4 minutes. The mixing chamber was sealed and vacuum was applied and mixing was continued for 16 minutes. Vacuum was released and the mixtures were removed from the mixer and allowed to equilibrate at room conditions before any testing was undertaken. Tests were performed as in Example 1. Table 2 below shows compositions prepared in this fashion with weight percentages of the indicated ingredients along with testing results for these compositions.

Table 2

4H PIB 40,000 molecular weight	6H PIB 60,000 molecular weight	Styrene-Isoprene- Styrene Copolymer	Polyacrylate Buffer	6 Hour Absorption g/cm ²	6 Hour pH	24 Hour Absorption g/cm ²	24 Hour pH	24 Hour Buffer Challenge pH
55.0%	0.0%	15.0%	30.0%	0.231	4.48	0.378	4.49	5.82
55.0%	0.0%	15.0%	30.0%	0.171	4.5	0.386	4.47	5.98
0.0%	40.0%	15.0%	45.0%	0.178	4.48	0.307	4.47	6.27
45.0%	0.0%	10.0%	45.0%	0.283	4.47	0.474	4.45	5.63
40.0%	0.0%	15.0%	45.0%	0.318	4.45	0.537	4.46	5.44
0.0%	50.0%	5.0%	45.0%	0.163	4.51	0.356	4.48	6.17
40.0%	0.0%	15.0%	45.0%	0.290	4.46	0.464	4.47	5.51
0.0%	55.0%	15.0%	30.0%	0.096	4.44	0.218	4.5	6.54
64.8%	0.2%	5.0%	30.0%	0.087	4.48	0.343	4.51	5.96
0.0%	44.6%	10.4%	45.0%	0.092	4.45	0.183	4.51	6.64
32.5%	32.5%	5.0%	30.0%	0.125	4.44	0.353	4.54	6.06
53.0%	0.0%	10.0%	37.0%	0.123	4.45	0.342	4.53	6.06
0.0%	65.0%	5.0%	30.0%	0.053	4.49	0.18	4.53	6.64
31.9%	26.6%	5.0%	37.5%	0.139	4.44	0.382	4.51	5.9
0.0%	47.5%	15.0%	37.5%	0.051	4.5	0.069	4.55	7.06
25.4%	32.1%	5.0%	37.5%	0.077	4.51	0.176	4.53	6.58
27.5%	27.5%	15.0%	30.0%	0.118	4.47	0.295	4.53	6.29
0.0%	50.0%	5.0%	45.0%	0.109	4.45	0.28	4.55	6.37
26.2%	33.8%	10.0%	30.0%	0.151	4.46	0.351	4.57	6.12
65.0%	0.0%	5.0%	30.0%	0.139	4.47	0.365	4.54	6.03
0.0%	65.0%	5.0%	30.0%	0.075	4.49	0.178	4.5	6.65
0.0%	55.0%	15.0%	30.0%	0.087	4.49	0.14	4.55	6.73
50.0%	0.0%	5.0%	45.0%	0.165	4.46	0.375	4.54	5.93
50.0%	0.0%	5.0%	45.0%	0.174	4.47	0.386	4.5	5.84

5 Example 4:

A third series of formulations based on PIB, Styrene-Isoprene-Styrene copolymer, polyethylene fibers and partially neutralized polyacrylic acid (35% Aronvis AH-106X) were prepared. A masterbatch composed of 50% PIB (Nippon 4H) and 50% Styrene-Isoprene-Styrene copolymer was prepared using a Brabender Type REE6 mixer at 140°C. The required weight of SIS was added to the mixer and was mixed at 36 rpm for 7 minutes. The required amount of PIB was added as mixing was continued at 36 rpm. The mixer speed was then increased to 100 rpm and mixing was continued for another 11 minutes. The masterbatch was removed from the mixer and cooled to room temperature before further use.

Compositions were prepared using a Brabender Type REE6 mixer at 85°C. The required amounts of polyethylene fibers and partially neutralized polyacrylic acid were pre-blended. The required amount of 50:50 masterbatch prepared as described above was added to the mixer and was mixed at 36 rpm for 4 minutes. The required amount of additional PIB was added to the mixer and was mixed at 36 rpm for 4 minutes. The pre-blended fibers and powder were then added over the course of 3 minutes while mixing at 36 rpm. Mixing continued for a further 2 minutes, following which the mixing chamber was sealed and vacuum was applied while mixing was continued for 12 minutes. Vacuum was released and the mixture was removed from the mixer and allowed to equilibrate at room conditions before any testing was undertaken. Tests

were performed as in Example 1. Table 3 below shows compositions prepared in this fashion with weight percentages of the indicated ingredients along with testing results for these compositions.

5 Table 3

Nippon 4H PIB	Styrene- Isoprene- Styrene Copolymer	PE fibers	Polyacrylate Buffer Aronvis AH-106X	6 hour Absorption g/cm ²	6 Hour pH	24 hour Absorption g/cm ²	24 Hour pH	24 Hour buffer challenge pH
48.9%	22.0%	2.0%	27.1%	0.213	4.64	0.293	4.63	6.07
55.0%	16.4%	3.8%	24.8%	0.183	4.65	0.184	4.65	6.21
53.0%	25.0%	2.0%	20.0%	0.065	4.61	0.072	4.68	6.81
51.0%	15.0%	4.0%	30.0%	0.281	4.64	0.359	4.65	5.89
55.0%	21.0%	4.0%	20.0%	0.040	4.61	0.034	4.68	7.04
52.8%	15.2%	2.0%	30.0%	0.265	4.59	0.332	4.63	5.99
43.0%	25.0%	2.0%	30.0%	0.239	4.64	0.326	4.59	6.03
55.0%	20.2%	2.0%	22.8%	0.099	4.63	0.091	4.64	6.68
41.0%	25.0%	4.0%	30.0%	0.257	4.75	0.356	4.58	5.92
47.4%	19.4%	3.1%	30.0%	0.297	4.75	0.390	4.6	5.89
52.0%	25.0%	3.0%	20.0%	0.053	4.74	0.062	4.65	6.81
48.3%	25.0%	4.0%	22.7%	0.116	4.74	0.186	4.61	6.29

Example 5:

A formulation based on PIB , Styrene-Isoprene-Styrene copolymer,
10 Polypropylene fibers and partially neutralized polyacrylic acid (35% neutralized Aronvis AH-106X) was prepared in a single step mixing process.

The composition was prepared using a Brabender Type REE6 mixer at 140°C.
The required weight of SIS was added to the mixer and was mixed at 36 rpm for 7 minutes. The required amount of PIB and mixing was continued at 36 rpm. The mixer
15 speed was increased to 100 rpm and mixing was continued for another 11 minutes. The required amounts of partially neutralized polyacrylic acid and Polypropylene fibers were pre-blended and the blend was added and mixing was continued for 4 minutes.
The mixing chamber was sealed and vacuum was applied and mixing was continued for 16 minutes. Vacuum was released and the mixtures were removed from the mixer
20 and allowed to equilibrate at room conditions before any testing was undertaken. Testing was done as in Example 1 and results are shown in Table 4 below.

Table 4

4H PIB 40,000 molecular weight	Styrene-Isoprene- Styrene Copolymer	Polypropylene Fiber Short Stuff Synthetic Pulp Y600F	Polyacrylate Buffer Aronvis AH- 106X	6 Hour Absorption g/cm ²	6 Hour pH	24 Hour Absorption g/cm ²	24 Hour pH	24 Hour Buffer Challenge pH
55%	14%	4%	27%	0.332	4.59	0.474	4.63	5.98

High molecular weight polymers such as those set forth above provide both enhanced pH buffering capacity and absorption with reduced skin irritation. The inventors have surprisingly discovered that low molecular weight acids, such as citric acid, are unsuitable for buffer systems in the present disclosure. Although such low molecular weight acids function acceptably as buffers, low molecular weight acid buffer systems cause unacceptable irritation to the user's skin for use as contemplated herein. When a buffering adhesive compositions similar to those of the disclosure but using a citric acid/citrate buffer instead of a high molecular weight polymer buffer was used in an adhesive dressing on human subjects, the subjects developed punctate ulcers under the dressing. The test results are shown below. Such an adhesive composition would be unsuitable for medical use. This result was both surprising and unexpected. The evaluation of a citric acid buffering system is described in Example 6 below.

Example 6:

In 1968, Lanman et al., reported that several days of repeated exposures produced a method to discriminate among mildly irritating cosmetic type products. With modification including shorter time periods (e.g., 21 days) this method has remained the standard test for determining a product's potential for mild cutaneous irritation. The methodology involves 21 consecutive daily applications under occlusion. A 1% sodium lauryl sulfate (SLS) solution applied on a non-woven pad served as the positive control while preservative-free 0.9% sodium chloride applied in a similar manner served as the negative control. This standard test was used to assess the irritation potential of various barrier formulations applied directly to skin for 21 consecutive applications. Because the barrier materials are self-adhesive, it was possible to partially differentiate between the contribution from irritation due to mechanical properties (skin stripping) and chemical irritation, by comparing irritation resulting from direct application with that observed when the barrier was isolated from the skin using a non-woven pad moistened with sterile normal saline as well as using barriers constructed with and without buffering material.

A sufficient number of normal volunteer subjects was recruited to ensure completion with 30. Each subject was exposed to all test materials and the sites were randomized using a standard Latin Square design. Graders were blinded to the identity of the materials. Materials were reapplied to the same site for 21 consecutive

days or until a discontinuation score was reached. The irritation data was treated using rank sum analysis. Rank sums range from 1 to 10 with higher numbers indicating more irritation.

Formulations used in the irritation testing are described below;

5 **Citrate Barrier**

Oppanol® B12	44.0%
TPC Group TPC1285 liquid PIB	7.0%
Polyethylene Fiber	3.5%
Pectin	8.5%

10 Sodium Carboxymethyl Cellulose	17.0%
Monosodium citrate Anhydrous	16.0%
Trisodium Citrate Dihydrate	4.0%

PAA Barrier

15 Oppanol® B12	55.0%
TPC Group TPC1285 liquid PIB	8.7%
Polyethylene Fiber	4.4%
Partially neutralized PAA	31.9%

20 Using this standard methodology, the irritation potential of the formulation containing 20% citrate barrier (mean rank 9.59) was similar to that of the positive control (mean rank 9.27). Only the barrier formulation containing citrate caused irritation accompanied by focal erosions (punctate lesions), which was different from the more uniform irritation typically observed with exposure to SLS. The barrier

25 formulated with PAA (mean rank 6.70) was significantly less irritating than either the positive control or the citrate buffer formulation. The slight irritation observed due to repeated exposure to the PAA barrier formulation was more uniform 'glazing' characteristic of repeated mechanical trauma, i.e., tape stripping. Both of these groups were different from the negative control (mean rank 2.68). The PAA buffer applied in

30 petrolatum (31.8% PAA in petrolatum) was non-irritating, indicating a lack of inherent chemical irritation due to repeated exposure to PAA. This observation is consistent

with the interpretation that the minor irritation observed with the barrier formulated with PAA is due to repeated mechanical damage.

An embodiment of the present disclosure contemplates the use of a high molecular weight polymeric buffer incorporated into the adhesive layer of a wound dressing. The wound dressing preferably includes a flexible outer layer such as a film. A hydrocolloid layer is on an inner side of the outer layer and contains the inventive high molecular weight polymeric buffer along with, optionally, an additional hydrocolloid such as CMC or pectin. As will be appreciated, the hydrocolloid layer is in direct contact with the wound bed.

In an embodiment, the wound dressing includes an adhesive component having a very high cohesive strength when hydrated to avoid potential disintegration of the dressing components in the wound bed. As will be appreciated, non-adhesive wound dressings incorporating the inventive buffer may also be possible.

A formulation suitable for a self-adhesive wound dressing would be, for example, formulation 7 in Table 2 (40% PIB, 15% SIS, 45% PAA) which has high cohesive strength due to the relatively high SIS content along with high fluid absorption and buffering properties, useful for managing wound exudate. Those of ordinary skill in the art would know how to use this formulation in preparation of a self-adhesive wound dressing.

Another embodiment of the present disclosure contemplates the use of a high molecular weight buffer incorporated into an ostomy skin barrier. The skin barrier may be permanently attached to an ostomy pouch (a "one step" or one piece arrangement) or may be separately attached using a flange clip system (a two piece arrangement). This embodiment of the disclosure will maintain the pH of the peristomal skin closer to the normal skin pH range of about 4.0 to about 5.5, thus reducing or eliminating the occurrence of irritation in the peristomal area.

Useful example formulations for ostomy skin barriers include those containing either polyethylene fibers or SIS. For example, formulation 3 of Table 1 combines desirable fluid handling ability with excellent pH control. Formulation 1 in Table 2 is an example of a formulation incorporating SIS with similar fluid handling and pH control. Those of ordinary skill in the art would know how to use this formulation in preparation of an ostomy skin barrier.

Also included in the present disclosure are methods of making and using the above-described high molecular weight polymeric buffer compositions. The making of the compositions of the disclosure is described above. The compositions may be used to manufacture any skin-adhering device by applying to a side or surface of the device an
5 amount of the composition effective to securely attach the device to the skin of the intended user.

While the invention has been described with reference to the preferred embodiments, it will be understood by those skilled in the art that various obvious changes may be made, and equivalents may be substituted for elements thereof,
10 without departing from the essential scope of the present invention. Therefore, it is intended that the invention not be limited to the particular embodiments disclosed.

What is claimed is:

1. An adhesive composition for a skin-adhering device comprising a high molecular weight polymeric buffer which provides both pH buffering and fluid
5 absorption.
2. The adhesive composition of Claim 1 wherein the high molecular weight polymeric buffer is a partially neutralized high molecular weight polymeric acid selected from the group consisting of polyacrylic acid, poly(2-alkyl acrylic acid),
10 copolymers of acrylic acid and 2-alkyl acrylic acid monomers, copolymers of acrylic acid and 2-alkyl acrylic acid monomers with maleic acid, and olefinic polymers substituted with side chains containing free carboxylic acid groups, wherein alkyl is from one to five carbons in length and may be straight chain or branched chain.
- 15 3. The adhesive composition of Claim 1 wherein the high molecular weight polymeric buffer is partially neutralized high molecular weight polyacrylic acid.
4. The adhesive composition of claim 3 wherein the degree of neutralization of the partially neutralized high molecular weight polyacrylic acid is from about 20% to about
20 40%.
5. The adhesive composition of Claim 1 which further comprises a pressure-sensitive adhesive selected from the group consisting of natural rubbers, synthetic rubbers, styrene block copolymers, polyvinyl ethers, poly(meth) acrylates (including
25 both acrylates and methacrylates), polyolefins and silicones.
6. The adhesive composition of Claim 5 wherein the pressure-sensitive adhesive is polyisobutylene.
- 30 7. The adhesive composition of Claim 1 which further comprises styrene-isoprene-styrene block copolymer.

8. The adhesive composition of Claim 1 which further comprises fibers selected from the group consisting of cotton fibers, polyethylene fibers, and polypropylene fibers.

5 9. A wound dressing comprising:
a flexible outer layer; and
a high molecular weight polymeric buffering adhesive applied to a side of the flexible outer layer, said adhesive providing pH buffering and fluid absorption.

10 10. The wound dressing of claim 9 wherein the high molecular weight polymeric buffer is a partially neutralized high molecular weight polymeric acid selected from the group consisting of polyacrylic acid, poly(2-alkyl acrylic acid), copolymers of acrylic acid and 2-alkyl acrylic acid monomers, copolymers of acrylic acid and 2-alkyl acrylic acid monomers with maleic acid, and olefinic polymers substituted with side chains
15 containing free carboxylic acid groups, wherein alkyl is from one to five carbons in length and may be straight chain or branched chain.

11. The wound dressing of claim 10 wherein the high molecular weight polymeric buffer is partially neutralized high molecular weight polyacrylic acid.

20 12. The wound dressing of claim 11 wherein the degree of neutralization of the partially neutralized high molecular weight polyacrylic acid is from about 20% to about 40%.

25 13. An ostomy skin barrier having an adhesive including a high molecular weight polymeric buffer to provide pH buffering and fluid absorption.

14. The ostomy skin barrier of claim 13 wherein the high molecular weight polymeric buffer is a partially neutralized high molecular weight polymeric acid selected from the group consisting of polyacrylic acid, poly(2-alkyl acrylic acid), copolymers of acrylic acid and 2-alkyl acrylic acid monomers, copolymers of acrylic acid and 2-alkyl acrylic acid monomers with maleic acid, and olefinic polymers substituted with side chains containing free carboxylic acid groups, wherein alkyl is from one to five carbons in length and may be straight chain or branched chain.

15. The ostomy skin barrier of claim 14 wherein the high molecular weight polymeric buffer is partially neutralized high molecular weight polyacrylic acid.

16. The ostomy skin barrier of claim 15 wherein the degree of neutralization of the partially neutralized high molecular weight polyacrylic acid is from about 20% to about 40%.

17. A method of making a buffering adhesive composition for a skin-adhering device that provides both pH buffering and fluid absorption which comprises combining a pressure-sensitive adhesive and a high molecular weight polymeric buffer in a single step mixing process.

18. The method of Claim 17 wherein the high molecular weight polymeric buffer is a partially neutralized high molecular weight polymeric acid selected from the group consisting of polyacrylic acid, poly(2-alkyl acrylic acid), copolymers of acrylic acid and 2-alkyl acrylic acid monomers, copolymers of acrylic acid and 2-alkyl acrylic acid monomers with maleic acid, and olefinic polymers substituted with side chains containing free carboxylic acid groups, wherein alkyl is from one to five carbons in length and may be straight chain or branched chain and the pressure sensitive adhesive is selected from the group consisting of natural rubbers, synthetic rubbers, styrene block copolymers, polyvinyl ethers, poly(meth) acrylates (including both acrylates and methacrylates), polyolefins and silicones, and mixtures thereof.

19. The method of claim 18 wherein the high molecular weight polymeric buffer is selected from the group consisting of high molecular weight polyacrylic acid and high molecular weight polymethacrylic acid and the pressure-sensitive adhesive comprises polyisobutylene.

5

20. The method of claim 19 in which styrene-isobutylene-styrene block copolymer is also combined with the high molecular weight polymeric buffer and the pressure-sensitive adhesive in the single-step mixing process.

10 21. The method of claim 20 in which polypropylene fibers are also combined with the high molecular weight polymeric buffer and pressure-sensitive adhesive in the single-step mixing process.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 13/27966

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61F 13/514, A61L 27/60, A61Q 17/00 (2013.01)

USPC - 424/78.06, 424/447, 424/448, 424/487, 523/111

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)

IPC(8)- A61F 13/514, A61L 27/60, A61Q 17/00 (2013.01);

USPC- 424/78.06, 424/447, 424/448, 424/487, 523/111

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents and NPL (classification, keyword; search terms below)Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest, PatBase (USPTO, EPO, JPO, WIPO, PCT), GoogleScholar (PL, NPL), FreePatentsOnline (USPTO, EPO, JPO, WIPO, NPL);
search terms: polyacrylic, acrylic, copolymer, skin, wound, ostomy, bandage, pH, buffer, neutralize, neutralisation, pressure, adhesive, polyisobutylene, fiber, fibrous, filament

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2007/0078197 A1 (SAMUELSEN) 05 April 2007 (05.04.2007), para [0014], [0018], [0027], [0032], [0047], [0048], [0051], [0056], [0058], [0061]-[0063], [0072], [0074], [0085], [0086], [0093], [0095]	1-3, 5-7,9-11,13-15,17-20 ----- 4, 8, 12, 16, 21
Y	US 2004/0073181 A1 (RAMASWAMI et al.) 15 April 2004 (15.04.2004), para [0032], [0057], [0063], [0071], [0076]-[0078], [0090]-[0092], [0096]-[0099], [0105]-[0108]	8, 21
Y	US 5,498,662 A (TANAKA et al.) 12 March 1996 (12.03.1996), col 1, ln 21-34; col 2, ln 21-50; col 3, ln 36-61; col 10, ln 47-49; col 14, ln 20-41	4, 12, 16
Y	US 2009/0258060 A1 (CLEARY et al.) 15 October 2009 (15.10.2009), para [0010]-[0165]	1-21
Y	US 6,639,120 B1 (WALLAJAPET et al.) 28 October 2003 (28.10.2003), col 3-20	1-21
Y	US 5,705,551 A (SASAKI et al.) 06 January 1998 (06.01.1998), col 2-12	1-21

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

* Special categories of cited documents:

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

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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

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"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

Date of the actual completion of the international search

29 March 2013 (29.03.2013)

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Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774