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CONTRACT NO:  DAMD17-90-C-0080

TITLE:  BIOMATERIAL ADHESIVES (SBIR 90.1)

PRINCIPAL INVESTIGATOR:  Ronald W. Gumbs

CONTRACTING ORGANIZATION:  Gumbs Associates, Inc.
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REPORT DATE:  March 1, 1991

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The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.
The purpose of this work was to develop a biologically compatible adhesive that will successfully maintain the adherence of a dermal dressing to moist (perspiring) skin on field personnel working in hot humid environments, without producing adverse reactions such as rash and itching. The project involved the design and synthesis of emulsion acrylic copolymers which were odorless and pressure sensitive. The water-insoluble adhesives contained hydrophilic units to permit strong bonding to wet human skin and still retain some water resistance to permit durability. During the emulsion polymerization, the amount of hydrophilic units incorporated in the copolymer was limited because of the large increase in the viscosity of the emulsion. As a result, the copolymer was prepared in solution in order to achieve better wet tack and water resistance. Peel adhesion and peel adhesion as a function of rate were satisfactory for a skin adhesive. The adhesive does not contain any residual monomer, a potential source of skin irritation.

Subject Terms:
Biocompatible Adhesives, Dermal, Hypoallergenic, Pressure-sensitive, Acrylic
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| DOE          | See authorities. |
| NASA         | See Handbook NHB 2200.2 |
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U.S. DEPARTMENT OF DEFENSE
SMALL BUSINESS INNOVATION RESEARCH (SBIR) PROGRAM
PHASE 1—FY 1990
PROJECT SUMMARY

Topic No. A90-188
Military Department/Agency: ARMY

Name and Address of Proposing Small Business Firm
Gumbs Associates, Inc.
11 Harts Lane
East Brunswick, NJ 08816

Name and Title of Principal Investigator
Dr. Ronald W. Gumbs, President

Proposal Title
Biocompatible Adhesives

Technical Abstract (Limit your abstract to 200 words with no classified or proprietary information/data.)
The purpose of this work was to develop a biologically compatible adhesive that will successfully maintain the adherence of a dermal dressing to moist (perspiring) skin on field personnel working in hot humid environments, without producing adverse reactions such as rash and itching. The project involved the design and synthesis of emulsion acrylic copolymers which were odorless and pressure sensitive. The water-insoluble adhesives contained hydrophilic units to permit strong bonding to wet human skin and still retain some water resistance to permit durability. During the emulsion polymerization, the amount of hydrophilic units incorporated in the copolymer was limited because of the large increase in the viscosity of the emulsion. As a result, the copolymer was prepared in solution in order to achieve better wet tack and water resistance. Peel adhesion and peel adhesion as a function of rate were satisfactory for a skin adhesive. The adhesive does not contain any residual monomer, a potential source of skin irritation.

Anticipated Benefits/Potential Commercial Applications of the Research or Development
It is anticipated that biocompatible acrylic adhesives will be available for bonding to the skin of active perspiring soldiers. The strong and water resistant adhesive bonds will allow the semi-occlusive dressing to function for at least three days without irritating the skin.

List a maximum of 8 Key Words that describe the Project.
Biocompatible Adhesives, Dermal, Hypoallergenic, Pressure-sensitive, Acrylic
TECHNICAL BACKGROUND

Need for a Biologically Compatible Adhesive

There is a need for a biologically compatible adhesive that will successfully maintain the adherence of a dermal dressing to moist (perspiring) skin on field personnel working in hot humid environments, without producing adverse reactions such as rash and itching. Current dermal adhesives do not possess the required degree of permanence.

Targeted Properties of the Adhesive

The adhesive should be compatible with and applied to semi-occlusive material to permit it to function successfully in keeping a dermal dressing adherent to the skin for at least three days on active perspiring soldiers. The purpose of the semi-occlusive material is to protect the underlying wound from exogeneous contamination (dirt, bacteria and water), yet allow adequate air and water vapor exchange to keep the wound moist without pooled fluid accumulation and permit the skin to breathe so that a rash doesn't develop. In addition to not interfering with these properties, the adhesive must be strong, water resistant, hypoallergenic, and nonirritating to human skin.

The characteristics of a good skin adhesive therefore are:

1. Absence of skin-irritating ingredients.
2. Good water resistance, so that the bond is maintained when skin perspires.
3. Sufficiently high cohesive strength to allow a clean removal of the adhesive from the skin.
4. Preferably high water vapor transmission rate to decrease the occlusivity of the tape.
5. Rheological properties to accommodate the skin movement without losing the bond and without excessive skin irritation mechanically.

Alternative Competitive Technologies and Drawbacks

Acrylic copolymer surgical tapes are widely used today, but they do not function very well on active perspiring soldiers. A copolymer of iso-octyl acrylate and acrylic acid (95/5 wt.%) on a microporous non-woven fibrous backing does not bond to wet skin. In addition, if the adhesive is wet, it is not tacky. On application in a dry field, it gradually peels away from the skin as the skin perspires.

Commercially available Stoma adhesives rely on a blend of a hydrophobic pressure sensitive elastomer, polyisobutylene, with water soluble adhesives such as carboxy methyl cellulose, pectin and gelatin for adhesion to moist skin. But the adhesion is only temporary since the perspiration gradually attacks the bond and eventually dissolves the adhesive.
Brief Outline of the Proposed Technology

The strategy pursued in Phase I was to tailor-make acrylic emulsion acrylic copolymers which are odorless, non-toxic, and pressure sensitive. The water-insoluble, biocompatible materials will contain the minimum concentration of hydrophilic units to permit strong bonding to wet human skin and still retain the required degree of water resistance to permit durability for at least three days on active perspiring soldiers. The ideal system is one that can be applied under water.

IDENTIFIED OBJECTIVES DURING PHASE I

The objectives as identified in the Phase I proposal were to:

1. Synthesize pressure sensitive acrylic copolymers which do not contain any residual monomers and which contain the optimum concentration of hydrophilic groups to permit adequate adhesion to moist skin and still retain a strong water resistant bond to human skin.

2. Characterize the copolymers and confirm the absence of residual monomers.

3. Evaluate the adhesives by measuring the dependence of peel adhesion on peel rate after demonstrating strong adhesion to moist skin and good water resistance.

METHODOLOGY

Synthesis

The emulsion polymerization process was used during Phase I for the copolymerization of the acrylic compounds. The objective was to achieve high molecular weights while keeping the concentration of soap at a minimum to maintain good water resistance. The polymerization was carried out in the presence of initiators, emulsifiers and buffers, in water as the external phase. Several different procedures were used initially in efforts to achieve 100.0% conversion of monomer to polymer, without any coagulation during the process. These include: a) passing a stream of nitrogen over the surface of the emulsion at 80-90°C for 30 minutes after all the monomer and initiator were added; b) increasing the concentration of initiator; c) carrying out the final phase of conversion over a period of several hours and d) using a redox system comprising of additional persulfate and a reducing agent such as sodium bisulfite or sodium hydrosulfite, with a small amount of a ferrous salt activator during vigorous stirring at the end of the addition of the monomer mixture.

A typical and optimum procedure for preparing the emulsion copolymers was as follows: A 1-liter four necked flask equipped with a mechanical stirrer, heating mantle, thermometer, nitrogen inlet, and two dropping funnels was initially charged with 300 ml of de-ionized water containing 1.0 gram of Triton X-405 (70%) and 0.5 gram sodium lauryl sulfate. After a nitrogen
purge for 15 minutes during which the mixture was stirred and heated to 80°C, a 200 gram mixture of monomers and an aqueous solution of 1.0 gram potassium persulfate dissolved in 10 ml of water were added separately over three hours at 80-85°C under nitrogen. At the end of the addition of the monomer and initiator, the temperature of the reaction mixture was increased to 95°C and maintained there for another hour. The reaction mixture was then cooled with continued stirring to room temperature.

Characterization

The solids content of the emulsion was measured by weighing a sample in a tared aluminum dish and heating at 105°C for 2 hours in a circulating oven. In addition, the amount of residual monomer could also be determined by boiling a weighed sample of the emulsion and recovering the steam distilled monomer.

The problem of residual monomer was solved early in the program and further characterization of the solid copolymers was unnecessary.

Evaluation

The following tests were conducted on each adhesive:

1. Wet Tack
2. Peel Adhesion
3. Water Sorption

Wet Tack

There is no satisfactory definition of tack in absolute units as, for example, elasticity and viscosity. The elusive nature of tack undoubtedly stems from the fact that it is a composite of these two parameters, if not more. For our purposes here, it was only necessary to determine whether the adhesive sticks to wet skin and this was ascertained by manipulating the film of the adhesive with wet hands. A qualitative and subjective measure of the degree of tack to wet skin was recorded.

Peel Adhesion

Two substrates, hydrated cellulose and nylon films, were most often used in 180 peel adhesion tests on the adhesives. Films were cast on one substrate and the other was moistened and bonded to the coated substrate with a five pound roller. After conditioning in a 100% relative humidity dessicator for 24 hours, peel adhesion tests were carried out using the Instron testing machine. Nylon was replaced with cotton cloth in some experiments late in the program, and in these experiments the water resistance of the adhesive was evaluated in a more rigorous fashion because of the porosity of the cloth, allowing penetration of the water to the bond. When cloth was used for both substrates, the peel adhesion gradually decreased over time.

After the peel adhesive strength was measured, the dependence of peel adhesion on peel rate was recorded for promising specimens.
Water Sorption

The water resistance of the bond of the adhesive between two substrates was of course measured during the peel adhesion tests on samples conditioned in high humidity environments. It was also necessary to determine the amount of water adsorbed on the surface and absorbed into the body of the adhesive during use. Thin films of known area, thickness and weight on microscope slide were immersed in distilled water for 24 hours at 37.5 °C.

COPOLYMERS SYNTHESIZED DURING PHASE I

The monomer feed concentrations, in weight percent, of successful emulsion copolymers prepared during Phase I are summarized in Table 1.

Table 1. Monomer Feed Concentrations of Emulsion Acrylic Copolymers

<table>
<thead>
<tr>
<th>Monomer</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>#6</th>
<th>#7</th>
<th>#8</th>
<th>#9</th>
<th>#10</th>
<th>#11</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Ethylhexyl acrylate</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>80</td>
<td>70</td>
<td>60</td>
<td>80</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>40</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Hydroxy ethyl methacrylate</td>
<td>10</td>
<td>20</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hydroxy ethyl acrylate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>15</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Acrylic acid</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>N-tert-Butyl acrylamide</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>19</td>
<td>19</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Vinyl Acetate</td>
<td>0</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

An important objective during Phase I was to graft copolymerize the acrylic monomers onto a water soluble homopolymer. To this end, polyvinyl alcohol was selected as the water soluble backbone, and the concentrations used in these experiments are listed in Table 2.

Table 2. Monomer Feed Concentrations used in attempts to Graft onto Polyvinyl alcohol

<table>
<thead>
<tr>
<th>Monomer</th>
<th>PVA-1</th>
<th>PVA-2</th>
<th>PVA-3</th>
<th>PVA-4</th>
<th>PVA-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Ethylhexyl acrylate</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Hydroxy ethyl acrylate</td>
<td>19</td>
<td>19</td>
<td>19</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Acrylic acid</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Polyvinyl alcohol</td>
<td>0</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>20</td>
</tr>
</tbody>
</table>
Because most acrylic surgical adhesives rely on the carboxylic acid group for adhesion to polar substrates and in view of the need for hydrophilic groups on the polymer chain, the effect of type of carboxylic acid was investigated. The monomer feed concentrations are shown in Table 3.

Table 3. Monomer Feed concentrations used in studying the effect of type of carboxylic acid on adhesion

<table>
<thead>
<tr>
<th>Monomer</th>
<th>A-1</th>
<th>A-2</th>
<th>A-3</th>
<th>A-4</th>
<th>A-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Ethyl hexyl acrylate</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Hydroxy ethyl acrylate</td>
<td>19</td>
<td>19</td>
<td>19</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Acrylic acid</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Methacrylic acid</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Itaconic acid</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maleic acid</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fumaric acid</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Several experiments were conducted where the monomer 2-ethylhexyl acrylate was replaced with butyl acrylate, ethyl acrylate and iso-octyl acrylate. Substitution of any of these monomers did not result in significant improvement in peel adhesion.

WET TACK

The function of the pressure sensitive adhesive is to provide instantaneous adhesion when applied under light pressure, and a skin adhesive further requires clean removal from the skin by a light pull. A pressure sensitive adhesive is characterized by having a built-in capacity to secure this instantaneous adhesion to a surface without activation, such as treatment with solvents or heat, and also by having sufficient internal strength so that the adhesive material will not rupture before the bond between the adhesive and the material and the surface ruptures. The capacity to obtain instantaneous adhesion is usually expressed as the amount of tack or tackiness.

During the course of this project we sought to obtain as much tack as possible without losing a significant amount of internal strength (cohesion). One very simple test which was used entailed coating one of the substrates with the adhesive and folding the adhesive surface against itself until there is a bond obtained between the two surfaces of the adhesive. The two surfaces are then pulled apart and the adhesive is then observed for the degree of leg, that is, the distance the material extends from the backing before both surfaces part. If the leg is too great, the adhesive lacks sufficient internal strength. Extreme leg is manifested by the formation of spider web-like fibers bridging the two surfaces. If, however, the surfaces pull apart with no more force than was needed to bring the two surfaces together, there is insufficient tack or adhesiveness.
We also sought an adhesive with permanent wet tack, internal strength (cohesion), resilience, cushioning power, and usefulness over a wide range of relative humidities.

Those copolymers without any hydrophilic monomers did not bond to wet skin. As the concentration of hydrophilic monomers increased, the degree of wet tack relatively increased. Increasing the amount of hydrophilic monomers in the emulsion copolymerization resulted in large increases in the viscosity of the emulsion, preventing the continued addition of monomer with adequate stirring. Late in the program it was determined that a solution copolymerization would permit higher concentrations of hydrophilic units and therefore better wet tack.

PEEL ADHESION

In general the peel adhesive strength of the adhesives was satisfactory. Values of 300 - 500 grams/cm were obtained to all substrates depending on the peel rate. Figure 1 shows the dependence of peel adhesion on peel rate for acrylic copolymer adhesive #8.
Figure 1. Dependence of peel adhesion on peel rate for an acrylic copolymer adhesive.
WATER SORPTION

The water resistance of the adhesives with acceptable wet tack was poor. Those adhesives with no wet tack had good water resistance. It is doubtful, however, that if these adhesives were applied to dry skin, they would possess any degree of durability once perspiration occurs. Because hydroxy ethyl acrylate units in the copolymer absorb as much as 20% water, resulting in a decrease in adhesion, it was necessary to replace half of this monomer with acrylic acid using a solution copolymerization process. The copolymer with 10% acrylic acid possessed acceptable wet tack and water resistance.

Emulsion copolymers containing N-tert-butyl acrylamide were not tacky wet or dry.

CONCLUSIONS

The major accomplishments of the Phase I work may be summarized as follows:

1. The major objective of demonstration of the feasibility of a biologically compatible adhesive that will successfully maintain the adherence of a dermal dressing to moist skin was achieved and confirmed with the successful synthesis and testing of an odorless, non-toxic, water-insoluble, pressure sensitive acrylic adhesive that bonds to wet human skin.

2. The water resistance of the adhesive was improved further by carrying out the copolymerization in an organic solvent and increasing the concentration of the carboxylic acid monomer.

3. The copolymers could be prepared without the presence of residual monomers, obvious and potential sources of skin irritation.

4. Peel adhesion to hydrated cellulose, nylon and cotton cloth substrates was satisfactory. So too was the peel adhesion as a function of peel rate.

5. Optimum composition of the copolymer based on the Phase I work is 2-ethylhexyl acrylate (45%), ethyl acrylate (35%), hydroxyethyl acrylate(10%) and acrylic acid (10%).

6. The water resistance of the adhesive may be further improved by replacing hydroxy ethyl acrylate with acrylic acid.