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A heightened awareness of problems with latex-based devices has intensified the search for alternative elastomeric materials and processing options.

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Dip Molding of Polyurethane and Silicone for Latex-Free, Nonallergenic Products

As more healthcare facilities require latex-free products to minimize the risk of allergic reactions among patients and staff, the demand accelerates for alternative elastomeric materials.

Tilak M. Shah

MEDICAL DEVICE MANUFACTURERS began looking for nonallergenic alternatives to natural rubber latex (NRL) more than a decade ago, when the number of reported cases of allergic reactions to latex started increasing dramatically. NRL is a highly elastic, very-low-durometer material exhibiting high tear resistance and high elongation. It has long been used to manufacture a wide range of healthcare products and components for medical devices. But as latex allergy has become a major occupational health problem for healthcare workers, nonallergenic alternatives to NRL are in greater demand to meet the needs of the medical device industry for latex-free materials.

THE MARKET FOR LATEX

Perhaps the most important market dominated by NRL is that of gloves and condoms. However, a number of soft, rubbery alternatives to latex have been developed and are being used, especially for gloves. The important ones are nitrile rubber, synthetic latex (which has no proteins), polyvinyl chloride (PVC), styrenic elastomers, polyurethane, and silicone. Dip-molded gloves produced from PVC, nitrile rubber, and styrenic elastomer have become popular. However, the use of PVC in medical products has come under fire recently amidst concerns about the use of phthalates as plasticizers and environmental concerns over disposal.

Photo courtesy of POLYZEN INC.

Low-pressure medical balloons have become a prominent application for dip-molded polyurethane or silicone.

For many years, polyurethane was limited to glove applications because of the high cost of formulations and its comparatively higher initial modulus, but recent advances in the formulation and processing of both polyurethane and silicone have resulted in these polymers becoming viable nonallergenic alternatives to NRL throughout the medical-products market. This is in part driven by new developments in dip molding of polyurethane and silicone, which have led to efficiencies in volume production. Solvent-based polyurethane formulations are growing as an alternative to latex for condoms, and novel water-based urethane formulations for gloves have been test marketed. Silicone is also rapidly becoming a preferred material because of its low initial modulus of expansion.

In addition, both polyurethane and silicone are growing in importance as materials for low-pressure balloons for cardiovascular, oncology, and urology devices because their properties can match those of latex, but without the negatives. While the cost of these two polymers is higher than that of other latex alternatives, cost is not a significant factor for such balloons. Other medical products in which polyurethane or silicone have successfully been substituted for NRL include surgical drains, catheter tubes, and various barrier products.

POLYURETHANES IN MEDICAL DEVICES

Polyurethanes were first discovered in the 1930s, but their potential in biomedical applications was not recognized until the early

1970s. Since then, this family of polymers has been used in the manufacture of pharmacologically inert devices for implantation in the body and in a variety of products for diagnostic and therapeutic procedures. Early obstacles to the use of polyurethanes as latex substitutes for medical devices included high manufacturing costs, inappropriate formulations, the prevalence of pinholes, and inadequate elasticity. Prior to the early 1990s, most polyurethane formulations featured hardnesses of 75 Shore A and harder for applications requiring superior mechanical properties and biocompatibility. The recent development of low-durometer, high-elongation formulations make them attractive alternatives to NRL.

Polyurethanes are thermoplastic rubbers made from isocyanates and are designated aromatic or aliphatic on the basis of the chemical nature of the diisocyanate component in their formulation. Aromatic and aliphatic polyurethanes share similar properties that make them outstanding materials for use in medical devices:

- High tensile strength (4000–10,000 psi).
- High ultimate elongation (250–700%).
- Wide range of durometer (72 Shore A to 84 Shore D).
- Good biocompatibility.
- High abrasion resistance.
- Good hydrolytic stability.
- Ability to be sterilized via ethylene oxide gas or gamma irradiation.
- Ability to retain elastomeric properties at low temperature.

When employed as part of an invasive device, both aliphatic and aromatic polyether-based polyurethanes soften considerably within minutes of insertion in the body, reducing patient discomfort and the risk of vascular trauma. The polymers can be colored using reactive dyes that chemically combine into the urethane chain, creating an unleachable covalent bond for color permanence and noncytotoxicity. Opaque colors are formed with high-density pigment powders that are thoroughly dispersed, providing uniformity of color.

The high strength and ease of processing of polyurethanes make them an excellent choice for soft-elastomer applications. The first commercial polyurethane medical product was a nonallergenic glove produced from film. Softer hybrid formulations were developed that enabled polyurethane to be used in typical latex medical product applications. Latex dip-molding technology was initially adapted to produce polyurethane barrier sleeves for dental instruments. Other advances that have made polyurethane a suitable replacement for latex in a variety of medical device applications today soon followed. These included water-based polyurethane latex and solvent-based urethane-urea formulations as well as urethane-silicone hybrids.

SILICONES AND BIOCOMPATIBILITY

First used in medical applications during the 1950s, silicones are among the most biocompatible synthetic materials available. Chemical analysis of silicones demonstrates low extractables and the absence of plasticizers and additives. Medical devices made of silicone exhibit low bacterial adhesion and thrombogenicity, making silicone ideal for surgical drains, feeding tubes, urethral probes, and other applications involving prolonged contact with body tissues. Contact hemolysis and complement activation are minimal when silicone devices come in contact with circulating blood. Like polyurethanes, silicones are excellent for low-durometer applications—strong, resilient, stretchable, and more stable than NRL.

Its flexibility, elasticity, resilience, and ability to be repeatedly autoclaved have made silicone a preferred material for many surgical devices. Given its high-temperature resistance, silicone tubing is suitable for electrosurgical and fiber-optic instruments. For critical dose administration of drugs or nutrition, silicone's ability to recover following repeated flexion and extension ensures accuracy and controlled stability in flow rates.

POLYURETHANE AND SILICONE PROPERTIES

Natural rubber latex has been difficult for device manufacturers to replace because of its many attractive properties in low-durometer applications. Chief among them are:

- High elasticity. Latex exhibits an elongation of more than 700%, even as much as 1200% in special formulations.
- Excellent recovery or memory. Latex is able to return to its original shape after it has been stretched to its maximum elongation.
- Low modulus of elasticity. Very little force is needed to stretch or elongate latex. For example, to achieve 50% elongation, only 80 psi is required.

However, latex has low chemical resistance: when exposed to hydrocarbons, oil, or grease, it disintegrates rapidly. It also exhibits poor UV resistance and quickly disintegrates when exposed to UV light. Table I compares some of the physical properties of dip-molded products made from polyurethane, silicone, and natural rubber latex.

Test	Polyurethane	Silicone	Latex
Tensile (psi)	3000–5500	800–1500	4400–4900
Elongation(%)	400–1000	600–1100	800–1200+
Tear strength (pli)	330–380	100–280	340–370
S tear (pli)	150–250	50–100	100–190
Tensile set @ 300%	2–10%	1–5%	None
UV resistance	Good	Good	Poor
Chemical resistance	Good	Good	Poor
Bondability	Good	Moderate	Poor
Allergic reaction	No	No	Yes

Table I. Comparative physical properties of dip-molded samples.

The elongation of polyurethane—while not as high as that of latex—is typically 400 to 500%, although special formulations have achieved 700 or 800%. Recently, however, polyurethane formulations with elongation as high as 1000% have been created. One of the biggest drawbacks for polyurethane is its higher modulus compared with NRL—that is, it requires more force

to expand or elongate to a given percentage than does latex. Polyurethane also exhibits a permanent set of from 2 to 5% when elongated within its elastic limits at 300%. Exceeding the limit produces a permanent set that could be much higher, though this is not typically a consideration in the medical device industry.

Silicone has a higher elongation than polyurethane and very good memory, making it the closest alternative material to latex in terms of these properties. Its modulus is higher than latex, but not significantly: to achieve 50% elasticity, 150 psi is required. In terms of chemical and UV resistance, silicone performs better than latex. A recently developed soft grade of silicone, which has a hardness of 20 Shore A, comes very close to latex in terms of modulus. Silicone formulations of 10 Shore A and 20 Shore A exhibit elongation of up to 1100%.

LOW-PRESSURE-BALLOON TECHNOLOGY

A prominent device application for polyurethane and silicone is in low-pressure elastomeric balloons, which can range from semicompliant to fully compliant models. Used primarily in fixation and occlusion, they are typically capable of being stretched from 500 to 600% of their size and then returning to their original dimensions. These components are different from high-pressure medical balloons, which are made of non- or low-compliant materials such as PET and nylon and are generally used to apply force in a variety of diagnostic and therapeutic procedures, including angioplasty and other dilatation applications. High-pressure balloons are molded to their final inflated size and shape from extruded preforms, and stretch very little. For insertion into the body, the balloon is wrapped around the shaft of a catheter in a low profile, then inflated with a saline or radiopaque solution by pressure from a syringe.

Latex, polyurethane, and silicone are used to produce low-pressure balloons, which are typically dip molded. Inflated by volume of air or liquid rather than by pressure, they are used for fixation of a catheter in a vessel or body cavity, occlusion of blood flow (sealing off a vessel during a procedure), drug delivery, and graft delivery, among other applications. In drug delivery, pores in the balloon enable the medication to be released slowly into the tissue. Other applications for these balloons include brachytherapy—the treatment of malignant tumors with radioactive material—and heat therapy with a heated solution.

Low-pressure balloons are also used in a variety of cardiovascular procedures. Applications include interaortic balloons, cardioplegia balloons (retrograde catheters), embolectomy/thrombolytic catheter balloons, intervascular and occlusion/transluminal catheters, catheters for minimally invasive bypass surgery, port-access catheters, and heart valve and thermodilation catheters. For ear, nose, and throat procedures, low-pressure balloon applications include tracheal-tube balloon and esophageal balloon catheters.

Latex-Free Balloon Formulations. Balloons made of polyurethane are well suited for bonding to catheter shafts, unlike latex balloons, which typically require several wraps of thread around the neck of the balloon and a drop of adhesive to keep it from unraveling. (One drawback of silicone is that it is just as difficult to attach to catheter shafts as latex.) Polyurethane has better resistance to chemicals, UV light, oil, and hydrocarbons than does latex. Under UV light, polyurethane may show some yellowing, depending on the grade. For example, aromatic urethane turns yellow under UV light but will not lose mechanical properties over the short term, though long-term exposure can cause property loss. Aliphatic polyurethane does not change color or lose properties under UV light.

OTHER DEVICE APPLICATIONS

Polyurethane and silicone dip-molded products are used in a variety of other device applications. In gastrourology, these include feeding tubes, enema cuffs, retention catheter balloons, bolster BPH catheters, urinary Foley catheters, biliary devices, stone-extraction balloons, and male urinary condoms. In neurology, devices dip molded from polyurethane or silicone include carotid shunts, embolic protective devices, and occlusion balloons.

Polyurethane and silicone are also used in a dip-coating process to apply a protective coating on medical devices, including stents for occlusion of diseased or cancerous tissue, esophageal stents, biliary stents, and stents for delivery of drugs and radiation. Scope tubes and baskets and wires used for blood-filter devices and emboli-collection devices are also dip coated. Coatings are also used for friction reduction, creation of antimicrobial or antithrombogenic surfaces, and production of hydrophilic or polar drug-delivery matrices.

DEVELOPMENTS IN DIP MOLDING

Dip molding of polyurethane and silicone is a relatively recent development. Unlike latex, which is water soluble, these polymers both require the use of a solvent to form a liquid phase. (A few companies are working on water-based polyurethane formulations, and the initial test market results are encouraging. If successful, this development would reduce the price from the current level for solvent-based systems.)

To dip mold a product, a mandrel in the shape of the object being molded is heated, dipped into the resin solution, then removed from the dipping tank. Mandrels can be machined from metal or formed from other materials. Metal is typically used for high-volume production. Glass mandrels produce a very smooth surface but are challenging to use because of their fragility.

Solution-processibile grades of polyurethane and silicone are formulated to be dissolved in solvents such as tetrahydrofuran, dimethylacetamide, methylene chloride, or a combination of several solvents. The viscosity of the solution depends on its solids content, which can be increased by adding more solids or decreased by adding more solvent until the desired consistency is attained. The mandrel should be lowered gradually into the solution to avoid solvent gassing or bubbles in the solution, which can result in pinholes and weakness in the finished product.

After dipping, the thin coating of the polymer that remains on the surface of the mandrel is allowed to cure, then is stripped off as a finished product. Multiple dipping steps build up wall thickness, with time, temperature, and speed of immersion among the factors affecting part consistency. Both silicone and polyurethane can be colored with the addition of pigment to the suspension.

Dip molding is a cost-effective process for low-volume pro-

AT RISK FOR LATEX ALLERGY

Many hospitals have adopted a policy restricting products made with natural rubber latex (NRL) in order to minimize the risk of latex-sensitive allergic reactions among patients and staff. NRL is manufactured mainly from the milky fluid of a rubber tree (*Hevea brasiliensis*) and contains variable amounts of proteins, which can be absorbed through the skin or inhaled. People who work frequently with medical supplies, such as nurses and lab technicians, are particularly at risk for extreme latex sensitivity because of their high exposure to rubber.

For some people, any contact with NRL can be life threatening. Sensitized workers can also develop occupational allergies—including respiratory, cardiovascular, and skin disorders—through contact with the proteins. Studies have also shown that cornstarch—which is added to latex gloves to facilitate donning and removal—as well as antioxidants, biocides, soaps, and other chemicals used in the processing of latex products can also contribute to sensitization.[1]

Reported cases of latex allergy among healthcare workers and patients began rising significantly in the late 1980s with the sharp increase in the use of latex medical products, especially gloves, as a precaution against the spread of HIV, hepatitis B, and other infectious agents. The U.S. Centers for Disease Control and Prevention recommended in 1987 that blood and certain body fluids be treated as potentially infectious. The use of barrier protection was subsequently required by the U.S. Occupational Safety & Health Administration (OSHA) bloodborne-pathogens standard.

Attention was drawn to latex allergy in the United States after latex retention balloons used in barium enema procedures were blamed for several fatalities due to anaphylaxis.[2] A high incidence of intraoperative anaphylaxis among children with spina bifida has also been attributed to the high prevalence of latex allergy among these children, probably induced by early and repeated exposures to NRL.[3]

Multiple centers in different countries, using a variety of assessment instruments and criteria, have found that between 8 and 17% of exposed healthcare workers are at risk for latex reactions. Among the general population, prevalence rates of up to 7% for antibodies to NRL allergy have been recorded.[4] Latex-allergy cases with severe skin and respiratory symptoms have been reported in dermatology, allergy, and pulmonary literature.

Allergic reactions to latex vary in severity from mild contact dermatitis (also known as Type-IV delayed hypersentitivity) to severe systemic (or Type-I) reactions—the most serious and potentially lethal. Symptoms range from mild irritation and delayed hypersensitivity in allergic contact dermatitis to immediate hypersensitivity in anaphylactic symptoms. Anaphylaxis is characterized by severe hypotension, rash, and bronchial spasm. Systemic allergic symptoms can include redness, itching, swelling of the lips and tongue, breathlessness, dizziness, nausea, abdominal pain, and shock.

In 1997, FDA issued a final rule that required labeling of medical devices containing NRL. Products and medical device packaging containing NRL are now required to carry a label declaring the presence of natural rubber latex and noting its potential for causing allergic reactions. FDA also prohibits the use of the word *hypoallergenic* on labeling of medical devices containing natural rubber.[5] In 1999, OSHA issued a technical information bulletin to alert field personnel to the potential for allergic reactions in some individuals using natural rubber latex gloves and other products made from the material.[6]

Last year, Congress established National Latex Allergy Week to raise public awareness about latex allergy and the importance of early detection, proper management, and proper prevention tactics. The resolution also establishes funding for research into the causes of latex allergy and for improved diagnostic, management, and prevention strategies.[7]

The Consumer Product Safety Commission (CPSC) is currently considering a petition to request a rule declaring NRL a "strong sensitizer" under the Federal Hazardous Substances Act. That designation indicates that a substance has significant potential for causing hypersensitivity. The petition claims that individuals have developed latex allergies or suffered allergic responses through exposure to NRL in consumer products. In toys and other products intended for children, the petition asks the CPSC to declare NRL a "banned hazardous substance."[8]

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duction of thin-film products, offering consistent wall thickness and uniformity, relatively low tooling costs, and fast setup for new product development. Barrier-type products with a wall thickness from 1 to 6 mil can be accurately manufactured with this process.

Because of solvent-handling considerations and a fairly long cycle time, the dip molding process for polyurethane and silicone balloons is relatively costly as compared with that for latex balloons. The cost-effective alternative for high-volume, preformed polyurethane balloons is blow molding, and, for silicone, liquid injection molding. For these alternative processes, the initial tooling cost is very high (similar to injection molding), but at volumes of 10,000 to 100,000 per month, the price per piece descends to a level comparable to that for dip-molded latex balloons. For nonlatex barrier sleeves, another innovative method is film welding, in which low-durometer, 1- to 2-mil urethane film is RF-welded into a variety of shapes and sizes for barrier-sleeve applications.

POLYURETHANE PROCESSING

For any of the above techniques, a thorough understanding of processing conditions is required when working with polyurethane resins. Polyurethanes are characterized as hygroscopic, since they absorb and react with moisture in the air very rapidly. Improper processing can significantly degrade the material, leading to defects such as voids, bubbles, discoloration, and other material defects in the finished part that could lead to product failure. Material degradation can be minimized through an understanding of the material property performance and potential degradation paths. Careful selection of equipment and optimization of process parameters will ensure the maximum retention of material properties.

CONCLUSION

The biocompatibility and the physical characteristics of polyurethane and silicone—high elongation, low modulus of elasticity, excellent recovery, and resistance to chemicals, oil, and UV light—equal and even exceed those of natural rubber latex. Such characteristics make these two polymer families especially suitable for products such as dip-molded, low-pressure medical balloons. Since both polyurethane and silicone are being manufactured at volume production rates, they can be considered viable nonallergenic alternatives to latex for a range of applications in the medical device industry.

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