Guayule, Neem, and Genetically Altered Tobacco Search for Niche Markets

Guayule rubber latex has the potential to be a hypoallergenic alternative to hevea latex. Neem pesticides are highly effective against target species, yet do not harm beneficial insects or animals. Researchers are beginning to tap into the tobacco plant's protein-producing capacity to make pharmaceutical and industrial compounds.

As stated in the June 1993 issue of this report, guayule rubber presently cannot compete with hevea rubber on price in traditional rubber markets. Establishing premium rubber-product markets, reducing agricultural production costs, and developing value-added products for guayule's other polymer and fiber materials are essential to its commercialization.

Due to the upsurge in demand for latex products in the mid to late 1980's, many foreign manufacturers increased output by cutting "washing" time, which removes proteins and other cell constituents from the latex. As a result, some people experienced allergic reactions to hevea latex products. Health care professionals who routinely wear rubber gloves and patients who undergo multiple surgeries are particularly susceptible. In 1992, more than 500,000 people in the United States were affected by this allergy. Recent studies of these allergic reactions confirm that several hevea proteins are the primary allergens. Since allergic reactions to these proteins can be severe, even fatal, and the number of sensitive people is increasing, alternatives are needed.

These proteins are not found in guayule. Therefore, people allergic to hevea latex could safely use guayule products. In two different clinical studies, a total of 62 hevea-sensitive individuals showed no allergic response to guayule rubber particles. However, they continued to be allergic to purified hevea latex. So, even if hevea-product manufacturers reduce the quantity of these proteins during processing, the small amount remaining would still cause allergic reactions in hevea-sensitive people.

To help commercialize guayule, researchers at USDA's Agricultural Research Service (ARS) have developed a continuous flow extraction process, amenable to industrial scale up, to isolate guayule rubber latex from the rest of the plant. ARS's research recently was supplemented by funding from the Advanced Materials From Renewable Resources Program, a cooperative effort by USDA and the Department of Defense for industrial product development.

The potential for guayule expansion into conventional latex products is promising. Over 300 medical devices and more than 40,000 products contain hevea latex. Surgical rubber gloves and condoms are just two examples. U.S. sales of surgical rubber gloves rose from $234.5 million in 1987 to $2.8 billion in 1992. The U.S. retail market for condoms rose from $103.3 million in 1987 to approximately $500 million in 1992. Considering the small portion of a condom's retail value attributable to higher the latex, higher priced guayule latex should be cost competitive with hevea latex. Furthermore, since manufacturers could market guayule condoms as hypoallergenic, they should be able to charge a higher price and possibly have a greater profit margin.

When guayule is processed for extraction of high-molecular-weight rubber *(HMWR)*, the major coproducts are resin and low-molecular-weight rubber (LMWR). While HMWR could be used for aircraft and land-vehicle tires and other traditional rubber products, value-added uses for resin and LMWR need to be developed. Polymer scientists at the University of Southern Mississippi have investigated several industrial uses for both coproducts. A marine coating that keeps barnacles from attaching to ships and a high-performance adhesive are two of the most promising prospects for guayule resin. Guayule LMWR can be used in high-quality polyurethane coatings, wood fillers, and wood finishes.

Scientists in Arizona, Texas, and California continue to improve agronomic practices for commercial guayule farming--soil nutrients, rainfall/irrigation, and planting and harvesting times, for example--in the hopes of improving yields and reducing costs. Plant breeding and genetic engineering approaches are also being used to improve guayule's natural rubber yields.

Neem Is a "Soft" Pesticide

Native to India and Burma, the neem tree has long been revered as "the village pharmacy" in many Asian cultures. However, some scientific work needs to be done before commercially successful products from neem can be used on U.S. food crops. Proponents of neem claim that the tree contains a powerful pesticide and repellent; is useful for cleaning teeth; is a natural contraceptive; and can heal wounds, infections, skin diseases, and fevers.

Neem-based pesticides are produced in many developing countries by crushing the seeds in a cloth bag and soaking the bag in a barrel of water. The water is then filtered and used as a spray. More modem refining processes can produce pesticides from neem seeds that can be applied as sprays, powders, or diluents in irrigation water.

Currently, neem-derived pesticides are being used in the United States on nursery and landscaping plants. Agri-Dyne Technologies and W.R. Grace have each released neem-based bioinsecticides and expect to enter the fruit and vegetable market once the Environmental Protection Agency approves neem derivatives for food crops.

Most promising is neem's potential to provide a "soft" pesticide--effective against target species and benign to most beneficial insects. Derivatives appear to be extremely effective antifeedants (feeding inhibitors), growth regulators, and repellents. Extracts appear to affect many different pests because of the wide variety of active compounds in the seed. In addition, neem derivatives appear to be completely benign to warm-blooded animals, including humans.

Many plants are able to absorb neem derivatives and transport them throughout the plant. Once absorbed, the pesticide cannot be washed off, the length of protection is often increased, beneficial insects that do not eat the plant tissue are not harmed, and new growth after application is protected.

Azadirachtin, the primary weapon found in neem, is responsible for about 90 percent of the tree's effect on insects and other pests. The chemical does not kill insects immediately--it repels them and disrupts their normal growth cycle. Affected insects often do not mature properly. For example, they do not reach advanced stages of the life cycle, certain features never develop (such as the wings or proboscis), and larvae never emerge from eggs. In addition, the compound repels females from laying eggs on sprayed plants and, in some cases, reduces the number of eggs that they lay. Azadirachtin also appears to be one of the strongest repellents ever found; thesmallest amount of the compound will cause insects to starve to death rather than eat the affected plant. Neem seeds contain 2 to 10 milligrams of azadirachtin per gram.

Meliantriol, vilasinin, and salannin are powerful antifeedants found in neem seeds. Small concentrations of these compounds can cause insects to stop eating altogether. Locusts and grasshoppers, California red scale, most beetles and flies, numerous destructive larva, weevils, fire ants, and several moth species are all greatly affected by these compounds. Other substances in neem apparently paralyze the "swallowing mechanism," thus causing the pest to die.

Neem seeds also contain two antiviral compounds, nirnbin and nimbidin. These are the first virus-inhibiting chemicals found in plants. They seem to be most effective against plant viruses carried by insects. The tobacco mosaic virus, which affects tobacco and some vegetable crops, has been susceptible to neem extracts in early trials. Further testing of neem's antiviral activity is needed before any strong conclusions can be made.

In tropical and sub-tropical climates, neem holds considerable potential as a plantation crop with numerous high-value products. The tree grows well in poor soils under extremely high temperatures and low rainfall. But it cannot withstand freezing, extended cold, or excessive amounts of water. Currently, almost all neem used in the United States comes from India, Africa, and Indonesia. Experimental plots have been planted in southern Florida, California, and Arizona.

Tobacco as a Protein and Drug Factory

Tobacco, long considered one of the major causes of cancer, may play a significant role in fighting that disease as well as other human ailments. Scientists at North Carolina State University (NCSU), along with RJ Reynolds Tobacco Company and Biosource Genetics, have field tested strains of tobacco and tobacco viruses that harness the plant's energy for production of anti-cancer and anti-AIDS drugs, human blood proteins, food-grade protein, and other pharmaceutical and industrial compounds.

According to Raymond J. Long, professor of Crop Science at NCSU, tobacco is readily amenable to genetic manipulation--"it's the white mouse of the plant world." The plant is ideal for producing large quantities of protein and protein products because the bulk of the plant's resources are aimed at developing leaves, not seed, fruit, or flowers as is the case with most food crops. Typical protein yields from tobacco are 2,200 to 2,600 pounds per acre.

Tobacco protein has been used to make an anti-AIDS drug and human serum albumin, a blood protein used to replace blood lost during surgery. Human antibodies and anti-cancer drugs are among the compounds being tested. Preliminary estimates suggest that production of such chemicals in tobacco could gross up to $12,000 per acre. However, farmers would probably not receive this entire amount. Current U.S. tobacco production grosses about $3,500 per acre. In addition, pharmaceuticals from genetically modified plants would have to compete with similarly modified bacteria and animals (see the animal products section).

Permanent gene transfer and the use of genetically altered viruses are two methods used to turn tobacco plants into chemical factories. Permanent gene transfer involves inserting a gene with the desired trait into a tobacco cell's DNA. The cell is then grown into an entire tobacco plant with the new genetic material. This plant is able to produce large quantities of the target chemical and can pass its newfound productive capability to its progeny.

At Biosource Genetics, biotechnologists have spliced into the tobacco mosaic virus and inserted instructions to make an anti-AIDS drug, human hemoglobin, and two enzymes. The altered virus was then sprayed onto a special field of tobacco and the infected plants began running the virus' genetic program. After harvest, the leaves were ground up and the target chemicals were extracted. Commercial use of this technology could occur by 1995. However, none of these new methods of protein production have been approved for commercial use by the Food and Drug Administration. [David Pace (606) 257-7272]