

**PRODUCTION AND PROPERTIES OF GUAYULE LATEX – THE
NATURAL SOLUTION TO LATEX ALLERGY**

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ABSTRACT

Natural rubber is an irreplaceable raw material vital to industry, transportation, medicine and defense, largely produced from clonal plantations of *Hevea brasiliensis* in South-east Asia. Additional rubber-producing crops are greatly desired to increase biodiversity, protect supplies, and provide a safe alternative for people suffering from Type I latex protein allergy.

Basic and applied research approaches were used to make the production of latex (yulex® latex) from *Parthenium argentatum* (guayule) a commercial reality. In contrast to *Hevea brasiliensis*, from which rubber latex is tapped by hand from laticifers, guayule latex rubber is contained within individual bark parenchyma cells. Processing involves disrupting these cells to release the rubber particles, and then purifying the latex. As in the *Hevea* industry, latex concentration can be achieved by centrifugation and/or by creaming agents. An artificially produced guayule natural rubber latex is then produced, under the material name of “yulex® latex”. The Yulex Pilot Plant has been constructed, optimized and automated, and extracts then purifies latex from guayule shrub without detectable losses. The natural rubber polymers in guayule latex are high molecular weight and products made from this material have the desired high performance properties. Because guayule latex contains very little protein, all of which is hydrophobic and bound to the rubber phase, and because none of the protein cross-reacts with Type I latex allergy to *Hevea* latex products, its use is initially aimed towards the high-value medical products marketplace. Clinical and performance trials continue to ensure that guayule processing provides a safe, high performance, non-allergenic natural rubber latex that is safe for human use.

INTRODUCTION

Natural rubber (*cis*-1,4-polyisoprene [9003-31-0]) is an irreplaceable, strategic raw material used in enormous quantities by industry, transportation, medicine and defense¹⁻⁴. The United States uses 14% of the global natural rubber supply, which it imports on a scale second only to its petroleum imports. Unlike fossil fuel, the U.S. has no domestic supply of natural rubber, and no longer has a stockpile. The high performance properties and cost effectiveness of natural rubber cannot be matched by synthetic polymers, and so natural rubber cannot be replaced by synthetics in many applications. In addition, in 2002, the three largest rubber-producing countries (Thailand, Malaysia and Indonesia, providing 72% of the global supply) formed a cartel to control production and prices⁴. Recently, two other rubber-producing countries (India and Vietnam) requested membership. Quite apart from the homeland security aspects of the natural rubber supply, the lack of genetic diversity and disease resistance puts the natural rubber industry at risk - natural rubber is currently produced largely from clonal plantations of *Hevea brasiliensis* in tropical South-east Asia, and the clones share a closely-related common ancestry. Leaf blight (*Microcyclus ulei*), a fungal disease, is the principle cause of the failure of the natural rubber industry in South America, and with modern, rapid transportation patterns, could be accidentally introduced into South-east Asia⁵. In addition, *Hevea* tropical latex products have given rise to the world-wide occurrence of life-threatening, IgE-mediated, latex allergy caused by the proteins in *Hevea* latex. Complete protein removal cannot be easily or cheaply achieved or proven, and, when attempted, negatively impacts latex product performance^{2,6,7}. Thus, additional rubber-producing crops are greatly desired to increase biodiversity, protect supplies, and provide safe alternative rubber products for individuals suffering from Type I latex allergy. Recent analyses by the International Rubber Study Group⁸ predict that natural rubber production will not keep up with demand leading to significant shortfalls by 2010, and a three million tonne per year natural rubber deficit by 2020.

Guayule as an Alternative Rubber Crop

At least 2,500 plant species are known to produce natural rubber but few of them do this in commercially-viable quantities or polymer molecular weights^{9,10}. In addition, few rubber plants have ever been grown on a large-scale as crops. A rare exception to this is guayule (*Parthenium argentatum* Gray), a rubber-producing woody shrub, native to the Chihuahuan desert of Texas and north central Mexico¹¹⁻¹⁷. Guayule should not be confused with “Parthenium weed”, or “Woody weed” (*Parthenium hysterophorus* L), a plant notorious for its invasive habit and for its production of an allergenic sesquiterpene lactone. Guayule has shown no signs of invasive behavior, despite field trials in many countries over several decades, and fortuitously does not produce the allergenic sesquiterpene lactone¹⁸.

Guayule rubber was produced commercially in the early part of the 20th century and was a major focus of the Emergency Rubber Project of World War II^{19,20}. These efforts

established that guayule produces high molecular weight rubber that can be used to make high quality tires, facts confirmed in the 1980's when guayule was cultivated and processed in response to the oil crisis and rising synthetic rubber production costs. Unfortunately, by the time the solvent extraction process, employed to extract guayule rubber as bulk rubber, was fully established, the oil crisis was over and guayule rubber was left to compete with the cheapest end of the tropical rubber market. Guayule rubber was much more expensive (*ca* 5x) and the commercialization effort came to an abrupt end²¹. The strategic necessity for natural rubber is not, of itself, sufficient impetus to produce rubber from guayule or other alternative rubber-producing crops.

A new opportunity for guayule arose in 1991 when the Food and Drug Administration issued a medical alert warning of Type I latex allergies to proteins in natural rubber products. The allergy arose because the enormously increased demand for latex gloves, caused by the institution of *Universal Precautions* in response to the AIDS epidemic, led to short-cuts in the glove manufacturing process²²⁻²⁷. The new products were made without washing the soluble latex proteins from the gloves – leaving them to be leached out by patients during glove contact with body fluids and mucosal membranes. The problem was compounded by the prevalence of single-use powdered latex examination gloves in hospital settings. Proteins from the gloves migrated post-manufacture to coat the corn starch powder donning agent. Rapid removal of gloves before the powder was dampened by perspiration led to the release of air-borne latex allergens – and hospital workers then constantly breathed them in inducing the high prevalence of latex allergies in this population. At least 400 medical and dental products are made with natural rubber latex and synthetic products lack the desired, and in some cases *required*, performance properties.

Guayule had not been investigated as a commercial source of latex because it does not make its rubber in the form of a tapable latex. Thus, if a cut is made into the stem of a guayule shrub no milky, rubber-containing emulsion bleeds from the incision. However, on a microscopic level, guayule, like latex-producing species, makes its rubber in small rubber particles floating in the aqueous cytosol. However, in guayule these are produced in individual bark parenchyma cells instead of in laticifers (networks of latex-containing living pipes made from anastomized cell systems). Extracting the guayule rubber particles, while maintaining them in the aqueous suspension, generates an artificially-produced natural rubber latex suitable for the manufacture of latex products. We have found that the rubber in the rubber that remains in latex form throughout the extraction and purification procedures is of consistent particle size distribution and of high molecular weight (at least 1 million g/mol).

RESULTS

Guayule Latex Proteins and Immunogenicity

Guayule latex contains very little protein (< 2%) compared with tropical latex and far fewer different proteins^{2,6,15,17,28}. Mouse and rabbit trials and human clinical trials, including ELISA (enzyme-linked immunosorbent assay), 1-D and 2-D immunoblots, skin-prick tests, RAST (radioallergosorbent) assays, and CAP assays of allergenic protein levels, have demonstrated that guayule latex proteins do not cross-react with anti-*Hevea*

latex protein antibodies at concentrations at least 1000x the amount of protein sufficient to cause a response to *Hevea* proteins^{4,6,28-33}. Reciprocal tests using animal antibodies (mice and rabbits) also demonstrated that antibodies deliberately raised against extracted and concentrated guayule latex proteins do not cross-react with *Hevea* latex proteins^{30,33}.

The method by which guayule latex is produced ensures that soluble proteins are washed from the latex during the purification process to undetectable levels. The remaining protein is hydrophobic and associated with the rubber particle membranes.

CONCLUSIONS

Commercial production of low protein, hypoallergenic guayule latex is a reality. Researchers have investigated a plethora of approaches seeking ways to best exploit and consume the crop^{4,46,47}, and research into new applications and uses for the latex, the resin coproduct and the lignocellulosic byproduct is continuing in private, academic and government laboratories. Guayule latex can be used to make high quality medical products and substitute for latex from *H. brasiliensis* and for the best of the synthetic polymers. However, latex characterization also has revealed novel properties that affect manufacturing processes and product quality. Some of these properties may lead to natural rubber products superior to those currently available. Continuing research to enhance yield, to exploit novel polymeric properties, and on the utilization of the coproducts and bagasse, will increase the profitability of guayule production. These approaches will allow conversion of the entire guayule crop to a plethora of products, while essentially eliminating the negative environmental impact of agricultural waste. Thus, guayule is positioned to rapidly expand as a model industrial crop feeding a new generation of biorefineries capable of producing a wide range of bioproducts and biofuels. The rapid crop cycle of guayule compared with *Hevea* also allows guayule to respond more rapidly to a changing marketplace. Guayule acreage expansion may well be the most practical means of preventing the three million tonne per year shortfall in natural rubber production predicted to occur by 2020 if nothing extraordinary is done⁸.