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Accelerator - Free Curing of Dip Molded Latex Films

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1. Introduction

An accelerator-free curing method (Anovel curing system@) has been developed for use with many existing latices, including natural rubber (NR), enzymatically deproteinized NR, guayule NR, synthetic polyisoprene (IR), polychloroprene (CR), and others. For the first time, an accelerator free peroxide based system can be used economically and effectively to cure thin films. Dip molded rubber films manufactured via the novel curing system are generally highly biocompatible, and free of the common allergenic agents responsible for Type IV latex allergies. NR films made via this novel curing system have exceptionally low levels of extractable proteins. While currently used vulcanization technology appears to be adequate for many dip molding applications, this new method should be strongly considered when the highest possible levels of biocompatibility are required. Such applications include implantable and indwelling medical devices, non-embryotoxic gloves for embryo transfer, catheter balloons, sheaths, etc. In addition, traditional dip molded products such as condoms and medical gloves can be improved with the incorporation of the novel curing system. While many traditionally compounded and cured latex films will not pass cytotoxicity tests, latex films produced by this new method will routinely pass. Products produced via this new curing method can effectively be manufactured without sulfur, accelerators, activators, and boosters. As a result, it may be possible to significantly reduce or potentially eliminate Type IV allergens in a variety of medical devices.

NR latex, without enzymatic treatment, exhibits substantially reduced to non-detectable levels of extractable proteins via the ELISA test method. It is proposed that certain allergenic proteins have been denatured and/or rendered water-insoluble during the curing step with the aid of heat and free radicals. Physical properties testing of various dipped films reveals tensile strengths and ultimate elongation values, which are substantially similar to those obtained by traditional dipped film vulcanization methods. Tensile set properties are generally more favorable than what can be obtained with traditional methods.

Prior attempts to use free radical vulcanization for latex films, including peroxide prevulcanization and radiation prevulcanization, have not been widely commercialized. Literature references clearly demonstrate that films produced in this manner have inferior aging characteristics and physical properties relative to traditionally cured latex films.

2. Background

2.1 Prevulcanization vs. Postvulcanization

Dip molded goods are traditionally produced from natural or synthetic rubber latex by 1) immersing shaped formers into a tank filled with compounded latex, 2) withdrawing the formers from the bath, 3) drying the water out of the film in a hot air oven, and 4) vulcanizing the resultant film at an elevated temperature. The individual rubber particles in the latex may have already been at least partially vulcanized (Aprevulcanized@) prior to the shaped formers being dipped into the latex. If the latex is not prevulcanized prior to the dip molding of the formers, then the latex process is considered to be a

Apostvulcanization@ process. Often, prevulcanized latex is used for dipping, and the dried rubber films are then further vulcanized in a postvulcanization process to obtain improved tensile properties. The use of prevulcanized latex has advantages, in that the wet and dry gel strength of the dipped film is generally improved, compared to latex that is not prevulcanized. The total process time is reduced, since only a limited amount of time (if any) is devoted to vulcanizing after dipping and drying. Details of these methods are well known. For example, a detailed description of latex dip molding with natural rubber latex is disclosed by Pendle.[1]

2.2 Superior Particle Integration

It is believed that particle integration may be improved upon if at least some postvulcanization is allowed to take place. The postvulcanization step is presumed to provide for covalent bonds between individual coalesced rubber particles, not just within the individual particles as is the case in prevulcanized films. In both of these processes, the latex particles are not necessarily uniformly vulcanized, since the outer surfaces of the particles are more directly exposed to the vulcanizing agents, in contrast to the interior of the particles. If the outer surfaces of the particles are more crosslinked than the interior of the particles, then a pseudo case hardening effect may have occurred. Some manufacturers allow latex to Amature@ in an effort to allow the crosslinks to become more evenly distributed throughout the film.

2.3 Prevulcanization Methods

As a general rule, sulfur is used as the primary vulcanizing agent for dip molded latex rubber components. Various accelerators, activators, sulfur donors, and boosters are necessary to properly compound these latices for use in traditional dip molding vulcanization processes. The prevulcanization of latex rubber without the use of these types of chemicals, or with no chemicals at all, by means of free radical crosslinking is well known. These methods rely on high-energy irradiation. NR latex exposed to high-energy irradiation is referred to as Radiation Vulcanized Natural Rubber Latex (RVNRL).

Often, a chemical sensitizer is used in combination with irradiation to achieve the desired properties. A detailed description of such a process has been described[2]. The tensile strength for rubber films made from this type of latex can be very good. No additional postvulcanization is done after the film is formed, so this process would be considered a prevulcanization process. While the tensile strength of dipped films made with this type of latex is adequate to meet the requirements of many dip molded rubber devices, such as surgical gloves, the tensile strength of these films is not as high as found in many traditionally prevulcanized latex films, which incorporate a postvulcanization step. The 100% tensile modulus values are also much lower than for conventional vulcanized NR latex films. There appears to be no known chemical method available to allow for true covalent bonding between integrated particles within these dipped films.

Another method of prevulcanizing latex by free radical crosslinking involves the use of organic peroxides and/or hydroperoxides. These types of latices are referred to as Peroxide Vulcanized Natural Rubber Latex (PVNRL). Numerous examples of this technique can be found in the literature[3, 4]. A typical process superheats natural rubber latex in the presence of organic peroxide(s). After cooling, films are cast and dried, yielding vulcanized rubber films with a tensile strength as high as 251 kg/cm^2 (3739 psi). In preparing the films, the films are only dried, and not subjected to any sort of post-drying vulcanization procedure. While this procedure reportedly works, to be commercially viable, large and expensive heated pressure vessels are required to prepare the latex. As with RVNRL, PVNRL also relies exclusively on the prevulcanization of the dispersed rubber particles. There appears to be no chemical pathway available to allow for covalent bonding of the former individual latex particles to form a truly integrated, pore-free latex rubber film. To avoid the use of pressure vessels, some PVNRL=s are made with the use of catalysts at lower temperatures[5]. Such methods generally produce lower tensile strength films, and leave chemical residuals in the films. Again, there is no means of integrating particles together via covalent bonds.

Previous attempts at incorporating some postvulcanization characteristics into RVNRL and PVNRL have required the use of additional vulcanization chemicals, including accelerators, activators, etc.

Postvulcanization with the use of radiation has not been commercialized for dipped latex articles, presumably due to the complexity of adding a radiation source directly next to a dip molding line. Peroxide postvulcanization has not been successfully done in the past because peroxide-containing films at elevated temperatures, exposed to an oxygen atmosphere, rapidly degrade. Many antioxidants are also rendered ineffective under these conditions.

3. Novel Curing System Process Description

3.1 Oxygen-Free Curing Environment

To overcome the above-mentioned problems associated with the all of the previously developed free radical curing systems, a new method was developed[6] to allow for the free radical postvulcanization of various latices via postvulcanization methods. The initial groundwork for this technology was conducted at Apex Medical Technologies, Inc. and was aimed at trying to improve the tensile properties of synthetic IR latex films. Even with the use of traditional compounding agents, it was our observation that it was very difficult to obtain suitable physical properties needed for the production of medical gloves unless large quantities and multiples types of accelerators and/or boosters were added. Traditional free radical curing methods were evaluated and found to be lacking, especially with respect to tensile strength.

Our development program led to the successful development of a free radical vulcanization process, which relies exclusively on a postvulcanization process. As mentioned previously, the main issue with postvulcanization of organic peroxide-containing films involves the degradation of the films during curing when exposed to atmospheric oxygen. By eliminating exposure of peroxide-containing latex films to atmospheric oxygen, it became practical to make excellent films via a postvulcanization process.

The elimination of oxygen is accomplished by using an elevated temperature oxygen-free environment, which can be created by several different methods. One particularly effective method is being recommended to licensees of this technology.

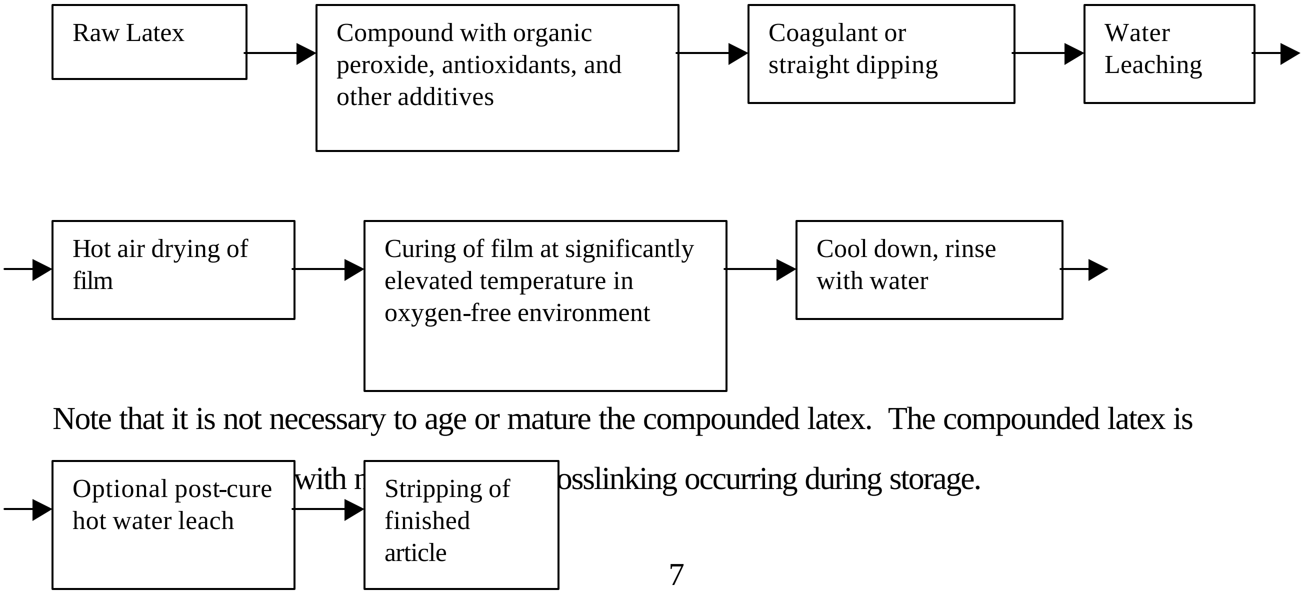
3.2 Elevated Temperature for Peroxide Homolytic Cleavage and Particle Integration

By excluding oxygen, and using high temperatures, it is possible to effectively utilize organic peroxides as latex rubber curing agents. For years, the use of organic peroxides has been widely used in solid rubber molding applications, and now it is possible to use similar formulations for latex dipped goods. While certain organic peroxides are especially preferred to create free radicals for crosslinking, it is possible to use other free radical generation methods to accomplish the same thing.

The temperature conditions used for curing are sufficiently high to thermally decompose the organic peroxide(s), and to simultaneously fuse the latex particles together. When dip molding latex articles, it is very advantageous to obtain good integration and bonding between the individual rubber particles. This helps to produce pore-free films, which are necessary to prevent the passage of pathogens, or other unwanted substances, through the wall of the dipped part.

3.3 Description of Novel Curing System Process Flow

A simplified flow diagram of the novel curing process is as follows:



Note that it is not necessary to age or mature the compounded latex. The compounded latex is with r osslinking occurring during storage.

4. Chemistry

4.1 Very Well Understood Chemistry

Organic peroxides undergo homolytic cleavage at elevated temperature. The resulting free radicals induce hydrogen abstraction of hydrogen atoms from the polymer backbone. These in turn create free radicals on the polymer backbone, which allow the chains to form carbon-carbon crosslinks with one another. These carbon-carbon bonds are stronger and more stable than those formed by sulfur crosslinking. Also, the bond is a very predictable one, unlike the many different types of carbon-sulfur bonds. The chemical character of the main polymer chain, however, is not changed, so it is still necessary to add anti-degradation agents to the compounds. It is also possible to add coagents during compounding to add a slightly different characteristic to some of the carbon-to-carbon bonds. The addition of certain coagents help to provide for the enhancement of certain specific physical properties, such are tear strength.

4.2 Peroxide Half-Lives

Organic peroxides break apart (homolytically cleave) in a very predictable manner. At any given temperature, organic peroxides have a half-life. This is the time it takes for one half of the currently present peroxide to homolytically cleave. In order to make sure that only trace amounts of organic peroxides remain after curing, it is important to keep the latex film at its predetermined curing temperature for the proper number of half-lives. For instance, after six half-lives, approximately 1.6% of the peroxide is left intact, and after eight half-lives only about 0.4% of the peroxide is left intact. A presumed safe target is eight or more half-lives. There are a very large number of organic peroxides, combinations of organic peroxides, and coagents to choose from. Some peroxides decompose at very low temperatures, such as dibenzyl peroxide, while others decompose at very high temperatures, such as 2,5-Dimethyl-2, 5-di (t-butyl-peroxy) hexane. Published tables of half-lives at various temperatures for a number of organic peroxides have been published. At least one software program is also freely available to help in calculating half lives and related information. It is important to use an organic peroxide which does not homolytically cleave at too low of a temperature, since it would then not be possible to dry the water out from the latex prior to vulcanization subjecting the film to severe degradation. It is preferable to choose a peroxide that can homolytically cleave rapidly at a temperature lower than the degradation temperature of the base polymer. By choosing the right peroxide and temperature combination, cure times of about two minutes to about nine minutes are conveniently used, while allowing adequate time for latex particles to fuse, and sufficient safety in the water drying process. However, it is clearly theoretically possible to achieve a full cure in a matter of seconds, if that is desirable.

For illustrative purposes Table 1 shows the relationship between temperature and half-life for 2,5-Dimethyl-2,5-di(t-butyl-peroxy)hexane.

Table 1: Temperature vs. Half-life of 2,5-Dimethyl-2,5-di(t-butyl-peroxy)hexane

Temperature		
Fahrenheit	**Celsius**	**1 Half-Life (seconds)**
300	149	1432
340	171	156
380	193	21
420	216	3.6

4.3 Peroxide Residuals and Breakdown Products

With the use of enough half-lives, very little organic peroxide remains in the cured film, however, there are some decomposition products. Therefore, it is important to choose a suitable peroxide to avoid any issues associated with unwanted breakdown products. One such organic peroxide, 2,5-Dimethyl-2, 5-di (t-butyl-peroxy) hexane, is especially well suited for biomedical applications due to its innocuous breakdown products. These breakdown products include methane, t-butyl alcohol, and acetone, which are volatile and tend not to stay in the cured films.

4.4 Types of Latices

Many, but not all latices can be cured with the novel curing system. To date, the following latex materials are known to be compatible with the novel curing system: natural rubber, enzymatically deproteinized natural rubber, guayule natural rubber, polychloroprene rubber, synthetic polyisoprene rubber, polyurethane, and nitrile rubber. One material known to be incompatible is butyl rubber. While traditional dip molding vulcanization methods are generally limited to partially unsaturated polymers only, it is now possible to cross-link fully saturated elastomers such as polyurethanes.

4.5 Tensile-Set Properties

The stability of the carbon-carbon bonds allows the vulcanized rubber materials to have better tensile set properties. This is especially true for synthetic polyisoprene latex and NR latex. For products such as catheter balloons, this is a very useful improvement compared to traditional curing techniques.

4.6 Clarity and Color

Synthetic IR latex can be made essentially water-clear. The color of cured NR latex films can also be improved, as there are few residual chemical compounds left in the rubber after curing. CR latex films develop amber to light brown coloration.

4.7 High Temperature Heat Stability

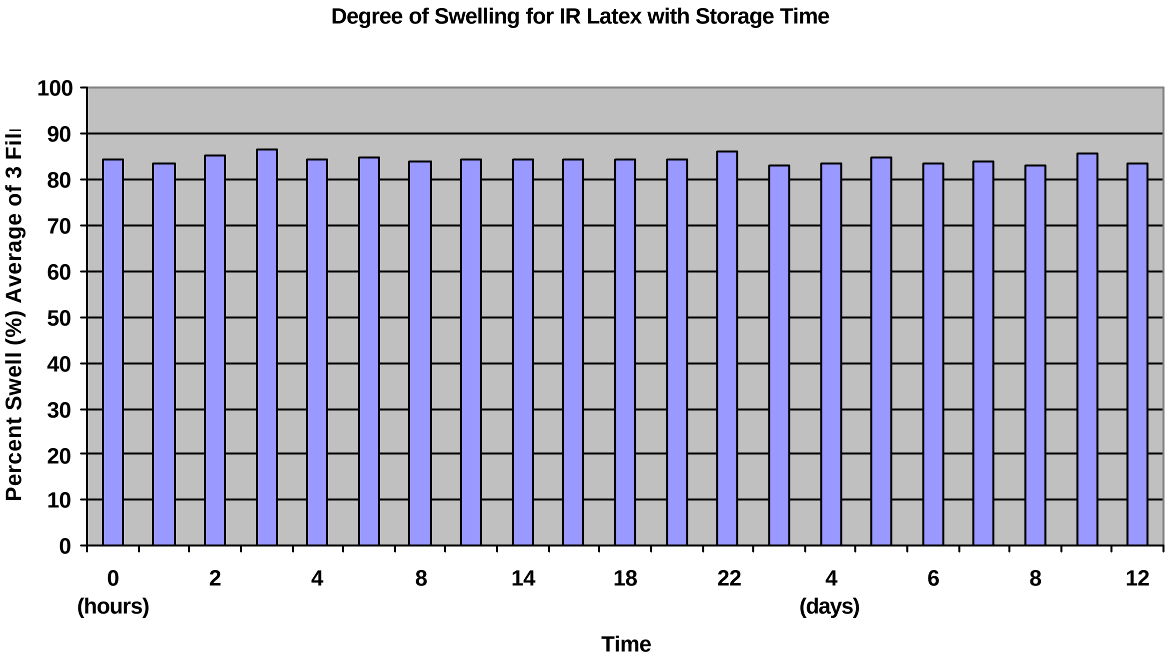
The carbon-carbon bonds are very thermally stable, unlike carbon-sulfur bonds. The normal polymer chain bonds are not changed with respect to their stability. This is important if the final dipped article is to be subjected to elevated temperatures during use. The use of coagents can also influence the exact high temperature behavior.

4.8 Compounded Latex Stability

It is possible to compound various latices with all of the necessary curative agent(s) in place without being concerned about the stability of the latex compound over time. With traditionally compounded latex, some crosslinking continues to occur over time. With the novel curing system, it is very practical to have the compounded latex to remain essentially unchanged with respect to degree of cure over a long period of time, since there is essentially no pre-curing taking place when stored until ambient conditions. Films made from compounded latex produce films with essentially the same state of cure in a manner, regardless of the age of the compound.

To prove this point, a short study was conducted which measured the state of cure as a function of storage time of the compound. Since solvent swelling is inversely correlated with degree of cure, it was used to demonstrate the degree of cure in this study. For this test, synthetic polyisoprene latex was utilized. Films were dip molded and cured at intervals ranging from one hour to 12 days. Small circular disks were cut from the cured films and were immersed in toluene for 30 minutes. They were then measured to determine the percent swell. As can be seen from the Figure 1, the state of cure remains very steady without regard to the time frame studied.

Figure 1



5. Biocompatibility Data

5.1 Cytotoxicity Test Data

There are many biocompatibility tests utilized by industry, government, and academia. Among the most sensitive biocompatibility tests are the cytotoxicity tests. One of the most common tests in this area is the agarose overlay test method. The testing presented in this paper was conducted by NAMSA=s Irvine, CA facility. In this test, a monolayer of L-929 mouse fibroblast cells is grown in culture on a test plate. The latex to be tested is cut into a one centimeter by one-centimeter square. Similar positive and negative controls are made to the same dimensions. Polyethylene is used as the negative control and polyvinyl chloride is used as the positive control. The test specimens are placed over the living cells, and the degree of lysis exhibited under the specimen and to the periphery of the specimen is observed after 24 hours of incubation. The degree of cytotoxicity is judged by the Azone of lysis. @ A zero zone of lysis is the best available score. Table 2 shows the results of the cytotoxicity testing conducted on various latex materials cured via the novel curing system.

Table 2: Cytotoxicity Test Results

Dip Molded Latex Material Tested	Zone of Lysis	Pass/Fail
Synthetic Polyisoprene	0	Pass
Polychloroprene	0	Pass
Enzymatically Deproteinized Natural Rubber	0	Pass
Low Ammonia Natural Rubber	0	Pass
Nitrile	0	Pass
Guayule Natural Rubber	0	Pass

As can be seen, for all types of materials tested, all passed with no zone of lysis. It can be inferred from these results that the crosslinked base polymers may not be toxic, and any toxicity registered in testing is more a function of the curative and compounding agents used. More testing would have to be done to prove this conclusively.

While many medical devices have only short-term contact with intact human tissue, many others are exposed directly to compromised or open tissue or mucous membrane. In these cases, it is advantageous to use a non-cytotoxic latex material.

5.2 Embryotoxicity Testing

One test, which might be considered even more sensitive than the above-mentioned cytotoxicity testing, is the Mouse Embryo Test. In this test, three sets of approximately 35 mouse embryos are exposed to the test article, a positive control, and a negative control. The percentage of these embryos that turn into blastocysts is recorded. To pass the test, 80% of the embryos must convert to blastocysts within 92 to 98 hours. This testing was conducted by Sage Biopharma, Inc., San Clemente, CA. The test procedure has been published8. The results are shown in Table 3.

Table 3: Embryotoxicity Testing Results

Latex Material	Embryos converting to blastocysts	Pass/Fail
Synthetic Polyisoprene - Chlorinated	97%	Pass
Synthetic Polyisoprene – Slip-Coated	97%	Pass

An example of where a low level of embryotoxicity is useful is in the field of assisted reproduction, such as GIFT, IVF, etc. Specific medical devices that can be of concern to practitioners in this area are medical gloves, probes covers, and other devices that are traditionally made from latex dipped films.

Primary Skin Irritation Testing

Primary skin irritation testing is important for screening and determining the suitability of a given material for skin contact applications. This test is conducted with a scoring of from zero to eight, with zero as the best score. Synthetic polyisoprene films cured with the novel curing system scored zero.

5.4 Nitrosamine Testing

Many accelerators used in conjunction with traditional sulfur curing of dipped films produce secondary amines as decomposition products. These secondary amines, aided by the presence of nitrosating agents in the polymer or atmosphere are sometimes converted to N-nitrosamines in the cured rubber films. Many, but not all, of nitrosamines formed during rubber curing are thought to be carcinogenic. Certain other N-nitrosamines are considered safe. However, the most conservative strategy to avoid the formation of nitrosamines in rubber compounds is to avoid the use of secondary amines, which can be transformed into N-nitrosamines. It is also best to avoid the use of compounds, which can become converted into secondary amines. It is significantly easier to accomplish this goal with the novel curing system, as there is no requirement, or compelling need to formulate with N-nitrosamine precursor chemicals. It is important to note that it is still imperative to review the make up of all the compounding agents to be certain that nitrosamine formation will not occur.

To demonstrate that nitrosamine formation was not a problem with the novel curing system, synthetic polyisoprene latex films were prepared and then tested for nitrosamines via the FDA alcohol extraction method. The results were acceptable, with 10 ppb or less of detected nitrosamines present.

6. Reduction of Water-Extractable Proteins From Natural Rubber Latex

6.1 Current Deproteinization Methods

Much work has been done with respect to significantly reducing the protein levels of NR latex. The traditional methods include double centrifuging the latex and/or exposing the NR latex to various enzymes[9]. Double centrifuging reduces the proteins mostly by reducing the serum concentration of protein. The enzymatic methods significantly reduce the molecular weight of the proteins by a digestion process. Most of the low molecular weight proteins, amino acids, and short peptide chains are extracted during the dip molding process. It is assumed that the remaining short chain peptides are essentially non-allergenic, due to the significant change from the initial chemical structure. For applications where high tensile strength combined with low cytotoxicity is not required, this strategy appears to work well. However, to achieve acceptable tensile strengths for certain applications, such as medical gloves, it is often necessary to use larger than desirable quantities of multiple types of accelerators to achieve the minimum desired physical properties. As a result, it is a challenge to achieve the desired combination of high tensile strength and low toxicity.

All of the above strategies involve additional cost. It is worth noting that the presence of protein in the latex films likely helps contribute to the strength of the cured latex films. By removing the vast majority of the protein, a significant reinforcing substance is also removed.

6.2 Guayule Latex - Alternate Proteins

An alternate strategy to reduce the level of allergic nature of NR latex films is to use guayule latex, which is inherently low in proteins, and indeed does not appear to contain the traditional proteins responsible for latex allergy[10]. Guayule latex is difficult to cure with traditional curative chemicals, and does not generally develop sufficient tensile strength for many applications[12]. It is also in short supply, but this may change soon. As will be shown later, the novel curing system allows for the development of excellent physical properties.

6.3 Novel Curing System Process - Free Radical Denaturization of Latex Protein

A surprise side effect of the novel curing system is the potential of free radicals and/or elevated temperatures to crosslink the native latex proteins, without necessarily removing them. The proteins become less water soluble, and with the almost certain loss of their native conformation, they become less allergenic. This is similar to the use of existing enzymatically treated DPNR latex, where some of the protein constituents are present, but in a more innocuous form. By retaining some remaining water-insoluble protein within the latex film in an innocuous, yet beneficial way, the natural reinforcing nature of the proteins can still be retained. Additionally, there is no additional cost associated with this method of reducing water-extractable proteins. While this strategy is quite novel in the field of latex proteins, it has been used preciously in the field of food allergies[11].

The discovery process occurred in several steps. First, a screening test was done to determine if denaturization did occur during the curing process. The second step to was to screen a large variety of curing conditions to determine which, if any, had the greatest potential for protein reduction. Third, a direct comparison was conducted to prove that the best conditions of the novel curing system produced lower amounts of water-extractable proteins than the best traditional sulfur-based curing conditions.

6.3.1 Step One - Initial Screening

Our first step was to try to establish that it was possible to denature and render the latex proteins non-allergenic. To do this, we chose a curing cycle for the novel curing system, which involved the curing of test films at 350°F for 9 minutes, without a postvulcanization water leaching process. The results from the ELISA test method were to be compared to the Lowry (ASTM D5712-95) method. It was hypothesized that a low score on ELISA, combined with a higher score on the Lowry test would support the concept of latex proteins being denatured during the curing process. Two similar test films were submitted to NAMSA=s Northwood, OH facility. The test results are summarized in Table 4.

Table 4: First Protein Screening Results

Film Type	ELISA Test Method	Lowry Method
Natural Rubber Latex film	Not Detectable	108 ì g/g

While not conclusive, this allowed us to continue our investigation.

6.3.2 Step Two - Larger Scale Screening

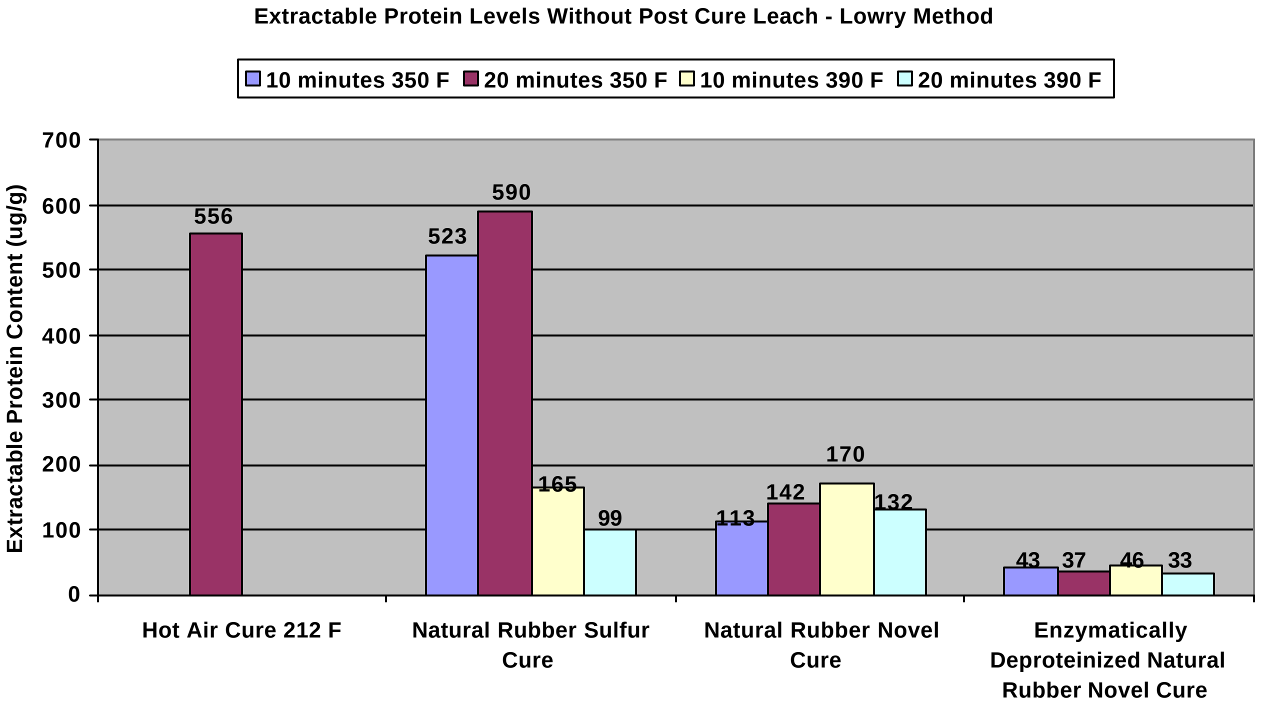
A large number of combinations of materials and curing conditions were screened to determine which conditions were likely to provide for low levels of water-extractable proteins. Since a non-detectable protein content via the ELISA method with the novel curing process was already established, the next step would be to focus on the Lowry method as the next logical screening tool to determine potentially optimal conditions. Included in this test group was a 20 minute wet gel water leach at approximately 60°C, but it did not include any postvulcanization leaching. The materials we choose to test were low ammonia NR latex, and enzymatically deproteinized NR latex. Low ammonia NR latex films were produced via the novel curing process, as well as by traditional sulfur hot air oven curing methods. For the traditional sulfur-cured films, we additionally used similar time and temperature profiles as provided for in the novel curing system in an attempt to better understand the effects of heat and free radical exposure. This was done to see if temperature alone was enough of a factor to make the proteins insoluble in water. The sulfur-based compounding ingredients were selected to give high tensile strength films, and included a proprietary mixture of the following: Zinc Oxide, Sulfur, ZMBT, ZDEC, and an antioxidant.

The results of the testing are shown in the Table 5 and Figure 2. As can be seen, the enzymatically-deproteinized latex cured via the novel curing system did the best, while the traditional sulfur hot air cured films did the worst. It can also be seen that several of the regular NR films cured with the novel curing system approached the same low levels of extractable protein. After studying this data, we proceeded to step 3 to try to confirm our ideas as to how to effectively minimize the level of extractable proteins for NR films.

Table 5: Lowry Extractible Proteins for Various Curing Conditions - No Post Cure Leach

Extractable Protein (µg/g) (average of three tests)			**Time (min)**	**Temp (°F)**
Deproteinized Natural Rubber Novel Curing System	**LA Natural Rubber Traditional Sulfur Cure**	**LA Natural Rubber Novel Curing System**		
43	523	113	10	350
37	590	142	20	350
46	165	170	10	390
33	99	132	20	390

Figure 2:



6.2.3 Step Three - Confirmation of Optimal Conditions for Deproteinization

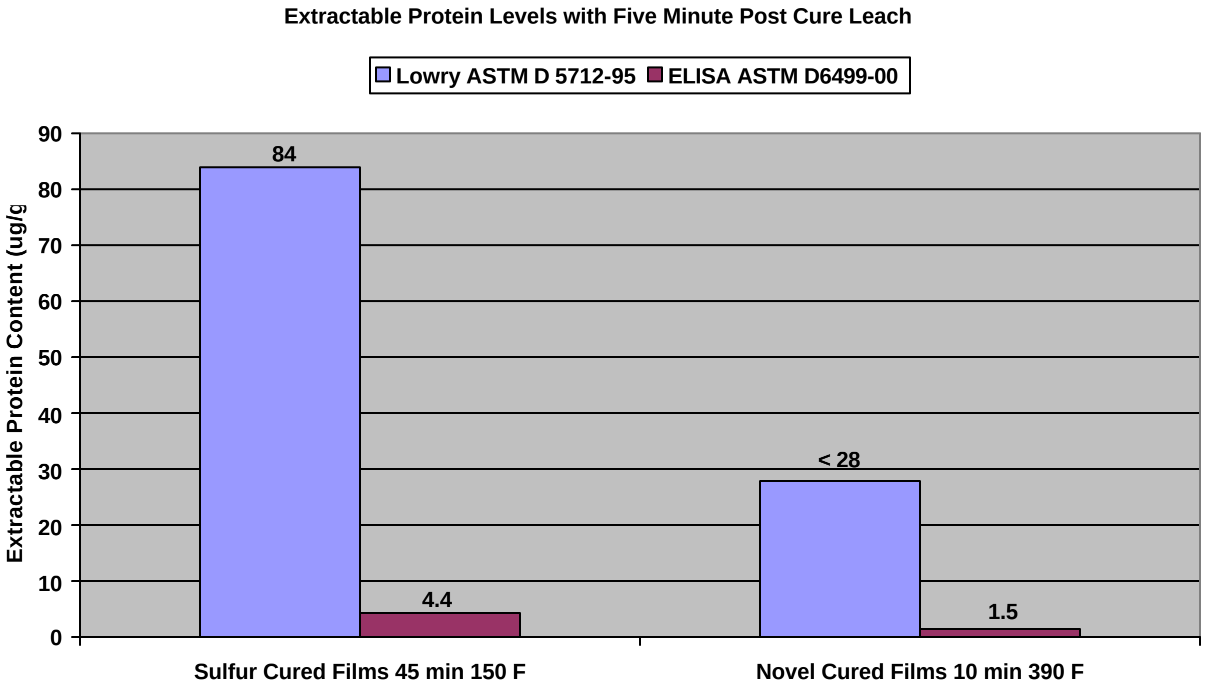
In this final step, we set out to prove that NR films cured with the novel curing process would be low in water-extractable proteins, even without first reducing the proteins with enzymes. We chose what we believed to be commercially viable conditions for both traditional sulfur-based curing and for the novel curing system processes. For the novel curing system, films were cured for 10 minutes at 350°F. The traditional sulfur-cured films were cured for one hour at 150°F in hot air. To help reduce protein levels even further, all of the film samples were leached in 70°C water for 5 minutes after vulcanization. Table 6 summarizes the test results. The testing was conducted by Guthrie Research Institute, Sayre, PA.

Table 6: Extractable Protein Levels - with Five-Minute Post Cure Leach

Film Type/Curing Conditions	Extractable Proteins - Lowry ASTM D 5712-95 Ì g/g	Extractable Proteins - ELISA ASTM D6499-00 ì g/g
Traditional Sulfur Cure 45 Minutes 150°F	84	4.4
Novel Curing System 10 Minutes 350°F	Not Detectable (< 28)	1.5

It is clear from Table 6 and Figure 3 that the level of water-extractable proteins is exceptionally low for the films produced by the novel curing system, without the need for enzymatic or other deproteinization steps.

Figure 3



7. Physical Properties Testing

7.1 Particle Integration and Uniform Crosslinking

While it is very desirable to have dip molded latex goods be highly biocompatible, it is also important to achieve excellent physical properties. As mentioned earlier, the novel curing process offers a number of advantages that can impart improved physical properties to the finished dip molded articles. In the author's view, two are most critically important. First, it is very important to have a uniformity associated with the crosslink density of the film. Second, it is important to have excellent particle integration combined with covalent bonding among all former particle interfaces. In light of the high curing temperatures and the curing conditions, which are very similar to solid rubber molding conditions, it is thought that the dry gel becomes partially molten while curing. This allows for particle integration and uniform curing.

7.2 Tensile Testing Data

Many different types and configurations of latex films have been produced by the novel curing system. It is essentially impossible to list all of the results in this paper, but some representative numbers are presented below. As can be seen from this data, the tensile strength is quite comparable to data published for traditional sulfur cured NR latex films. For other films, it is thought to be superior. It is especially noteworthy in cases where sulfur curing systems do not work very well, such as with guayule rubber, deproteinized NR, and synthetic polyisoprene.

7.2.1 Natural Rubber

In Step 2 of section 6.3.2, multiple sulfur-cured and novel curing system NR latex films were prepared. Tensile testing was conducted on all of the various cured films following the procedures of ASTM 3492. Results of this testing are presented in Figure 4. Film thicknesses were close to those used in surgical gloves.

Figure 4:

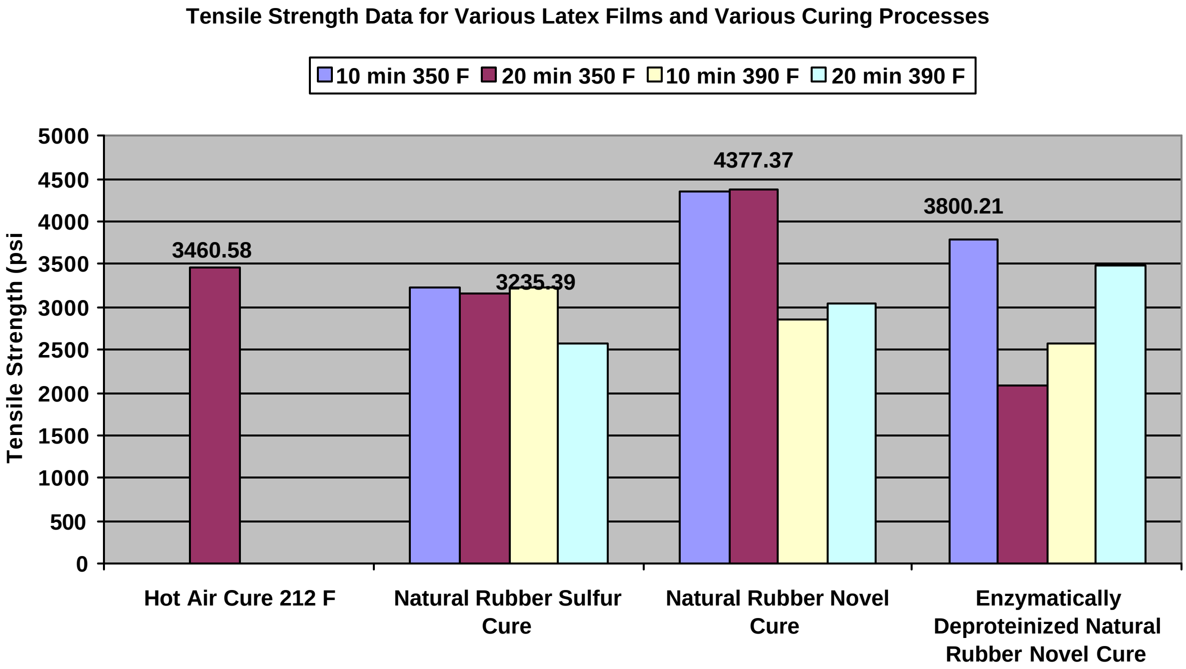
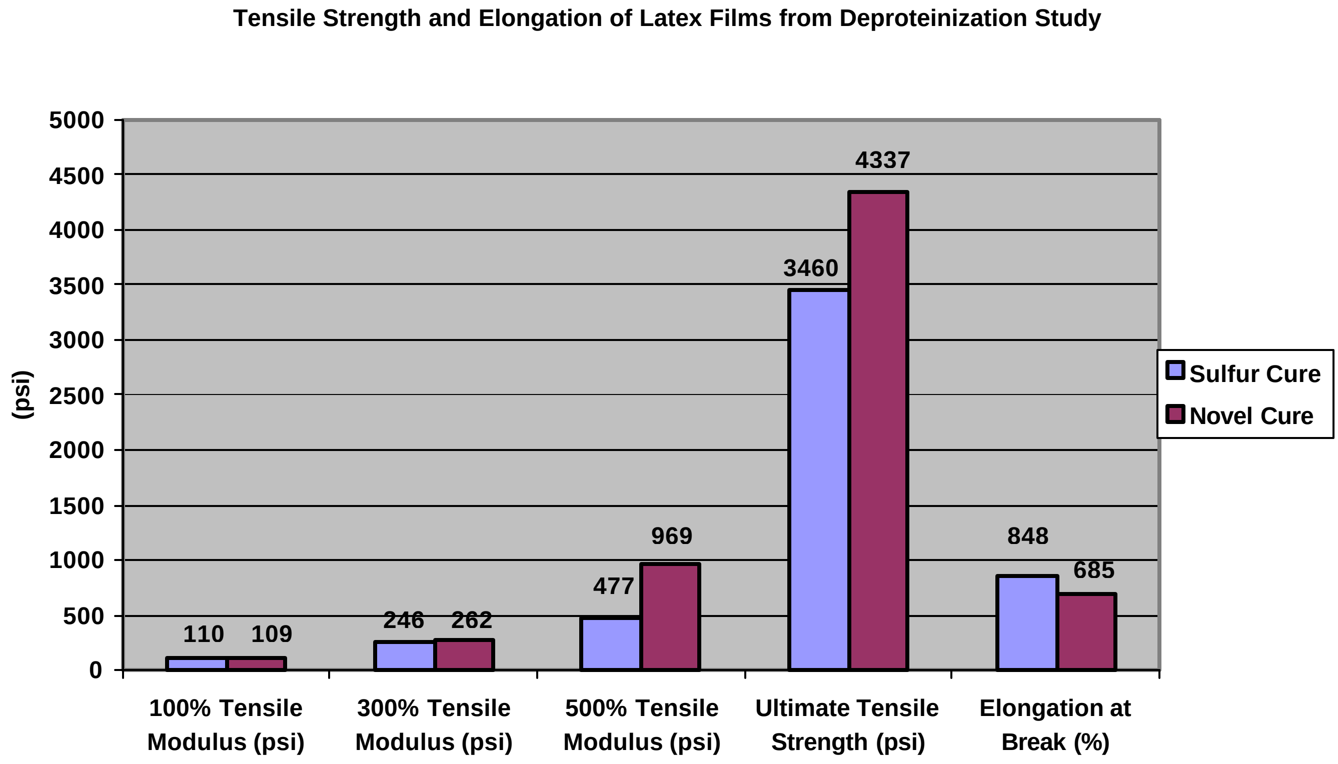


Figure 5 shows the tensile testing results conducted on those films produced in Step 3 in Section 6.3.3, which were deemed as the most commercially viable conditions.

Figure 5:

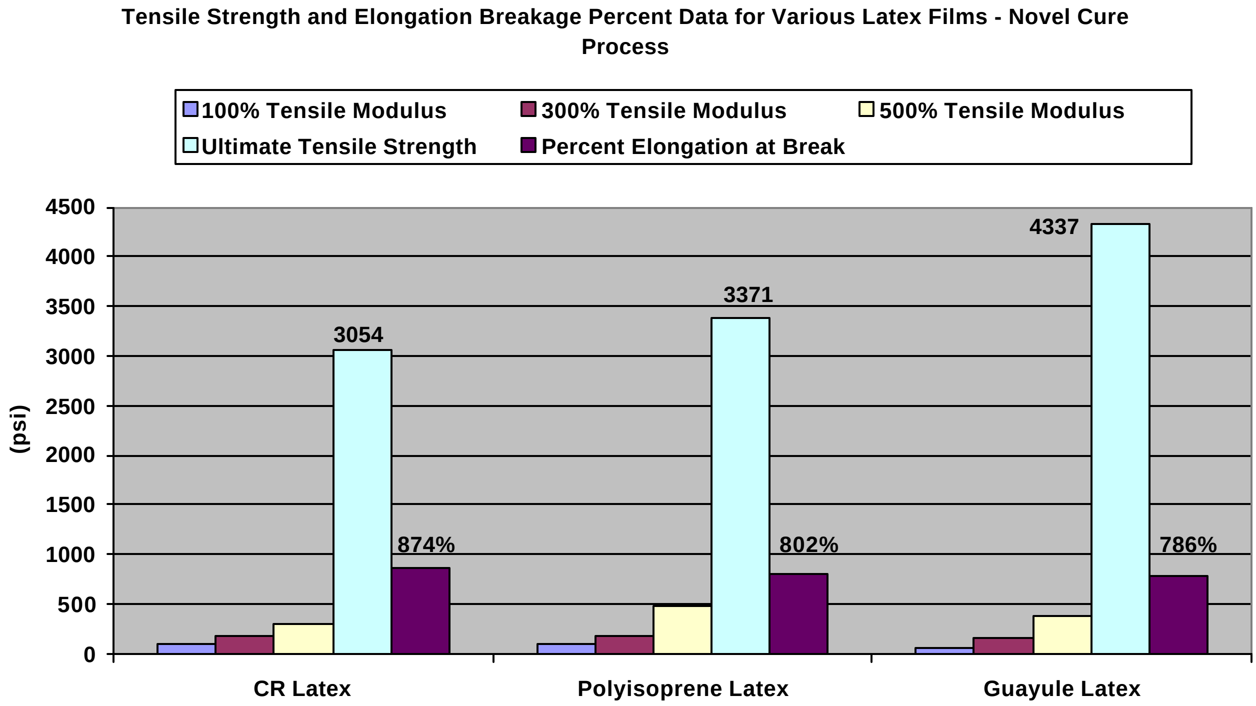


As can be seen, the novel curing system produced better tensile strength than this particular sulfur cure system. The tensile values are believed to be similar to those published by others for high quality sulfur-cured films.

7.2.2 Synthetic Polyisoprene and CR Latex

Some typical tensile data for various alternate lattices is shown in Figure 6. For the synthetic polyisoprene and CR latex that follows, these samples were made at approximate condoms thickness (about .003"). The guayule films were made at surgical glove thickness. These films were cured for 9 minutes at 350ºF. Tensile testing was conducted in accordance with ASTM D3492.

Figure 6:

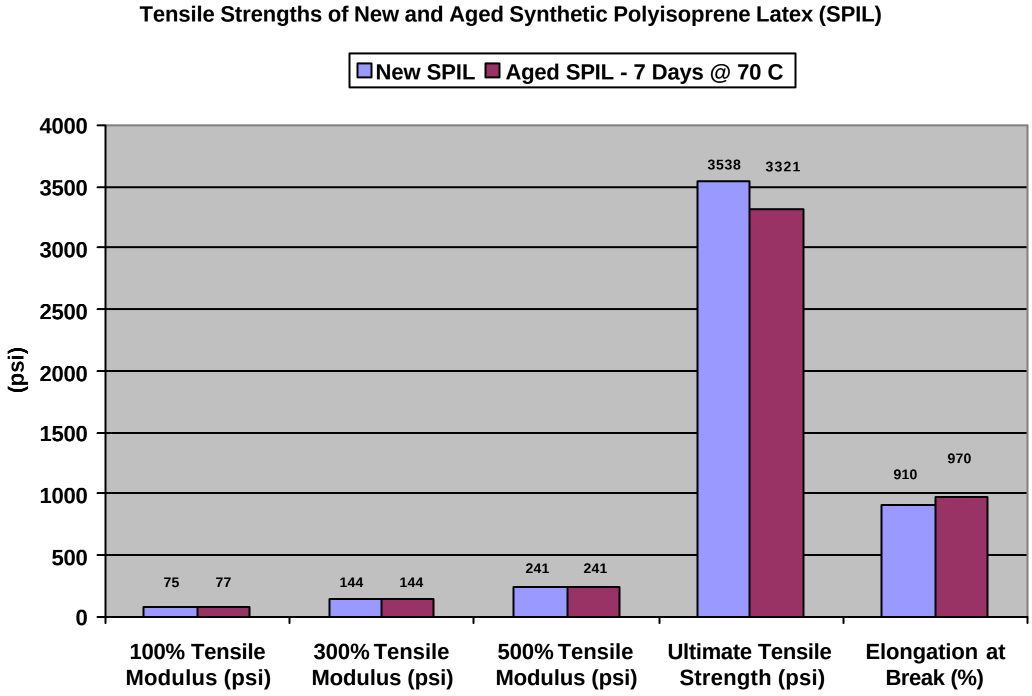


7.3 Accelerated Aging Testing

It is very important for dipped latex films to retain the majority of their tensile properties after being subjected to accelerated aging. For purposes of illustration, an aging test was conducted on synthetic IR latex films made at surgical glove wall thickness. Tensile testing was conducted in accordance with ASTM D3492. As can be seen in Figure 7, there is very little change in tensile properties after accelerated aging. These films were exposed to open air, making the test even more severe than what is required by published standards.

The stability of carbon-carbon bonds is superior to that of carbon-sulfur type bonds, which may help contribute to the aging characteristics. Residual chemicals are also minimal, which probably also helps. Even with these considerations, it is still necessary to use an antioxidant when formulating, as the backbone of the polymer itself is still subject to normal degradation mechanisms.

Figure 7:

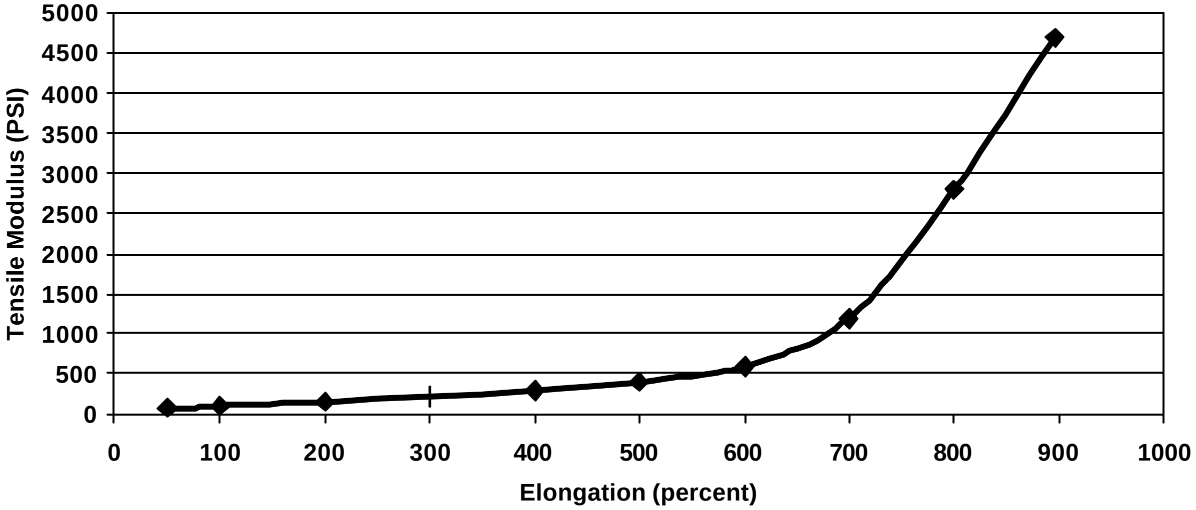


7.4 Coagents

In some instances, it is necessary to have exceptionally high tensile strength properties to meet the needs of certain dip-molded products. When these exceptional properties are required, it is possible to add small amounts of coagent(s) to the compounded latex. The presence of the coagent(s) provides for a slightly different type of crosslinked network than would otherwise be present with only an organic peroxide present. One target product category is a synthetic polyisoprene latex condom possessing exceptional tensile strength. The following graph shows the tensile strength and elongation characteristics of one particularly well-suited material for use in producing condoms.

Figure 8

Stress - Strain Graph for
Polyisoprene Latex - Novel Cure with Co-Agent



8. Concluding Remarks

The accelerator free novel curing system described in this paper can contribute to the production of latex films with excellent toxicity profiles combined with outstanding physical properties. The potential exists to produce dip molded medical devices, such as condoms, gloves, and catheter balloons with very low potential for causing type IV latex allergies. The longstanding issues of nitrosamines can be readily dealt with. It is now possible to make NR latex films with very low levels of extractable antigenic proteins, without the need to first enzymatically treat the latex. For decades, dipped latex films have had to take a back seat to expensive biocompatible elastomers when it came to important biomedical applications. The novel curing system can now allow latex films to become state of the art biocompatible biomaterials.

References:

1) *Dipping With Natural Latex*, 1995, The Malaysian Rubber Producers= Association

2) *Semi Industrial Scale RVNRL Preparation, Products Manufacturing and Properties* Zin, Wan Manshol Bin W. ABBREVIATED JOURNAL TITLE- Radiat. Phys. Chem. VOL. 52 NO. 1-6 1998 PP. 611-616 DOCUMENT TYPE- Journal ISSN- 0969-806X

3) US Patent 2,868,859, Geoffrey Scott, 01/13/59, Entitled *Curing Natural Rubber Latex with a Peroxide*

4) US Patent 2,975,151, Walter S. Ropp, 03/14/61, Entitled *Vulcanization of Latex with Organic Hydroperoxide*

5) US Patent 3,755,232, Bruce K. Rodaway, 08/28/73, Entitled *Prevulcanization of Rubbers by Hydrogen Peroxide and An Activator*

6) US patent application, Serial Number 09172965

7) *The Vanderbilt Latex Handbook*, Page 110, Third Edition, published by R.T. Vanderbilt Company, Inc., Norwalk, CT, USA

8) Quinn, et al., Fertility and Sterility 41:201, 1984 and 44:493, 1985

9) Perrela *Enzymatically Treated Natural Rubber Latex: A Practical Approach*, International Latex Conference paper presented July 21, 1998

10) Siler, Cornish, Hamilton *Absence of Cross-Reactivity of IgE Antibodies from Subjects Allergic to Hevea brasiliensis Latex with a New Source of Natural Rubber Latex from Guayule (Parthenium argentatum)*. J Allergy Clin Immunol 1996;98:895-902

11) US Patent 4,078,093 Girsh, et. al, entitled *Hypoallergenic Chocolate*, Issued: March 7, 1978