Macromolecular photoinitiators enhance the hydrophilicity and lubricity of natural rubber

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ABSTRACT: A mild and facile strategy to coat natural rubber (NR) with a hydrophilic coating is described that uses light and photoinitiator copolymers. Five high molecular weight photoinitiator copolymers, composed of hydrophilic (e.g., 2-hydroxyethyl acrylate [HEA], poly(ethylene glycol) [PEG], N-vinylpyrrolidone [NVP], N-isopropylacrylamide [NIDAM], and acrylic acid [AA]) and hydrophobic benzophenone (BP) units, are synthesized and evaluated for coating NR on UV irradiation. When the HEA/BP, NVP/BP, and AA/BP macromolecular photoinitiators attach to the NR surface, the latter becomes hydrophilic. The resulting hydrophilic coatings on NR sheets are analyzed via FT-IR spectroscopy, scanning electron microscopy, atomic force microscopy, contact angle measurements, and transwell cytotoxicity assays using NIH 3T3 fibroblast cells. The addition of high molecular weight hydrophilic polymers (e.g., polyvinylpyrrolidone and poly(2-methacryloyloxyethyl phosphorylcholine)) to the coating further enhances the coating's hydrophilicity and lubricity. The application of these non-cytotoxic, hydrophilic, and lubricious coatings on NR expands current applications and usage of NR. © 2016 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 2016, 133, 43930.

INTRODUCTION

Products using natural rubber (NR), or latex, possess favorable chemical, physical, and rheological properties, including elasticity, low heat resistance, and chemical resistance to polar organic solvents (e.g., ethanol).[1–3] Due to these advantages, NR is used in a variety of consumer goods (most notably, vehicle tires), laboratory products, and medical devices. In fact, the demand for NR is projected to be 29 million metric tons this year.[4,5] NR is cultivated from *Hevea brasiliensis*, also known as the rubber tree, and contains unsaturated C=C double bonds (*cis*-1,4-polyisoprene).[2,3] Bulk properties of NR are modified for improving wet-grip characteristics for tire tread applications[6] and for tuning the conductivity for sensor and electromagnetic shielding applications.[7] The double bonds in NR contribute to NR's hydrophobic properties which renders it non-compatible with blood, leading to the irreversible adsorption of biological components (e.g., proteins and platelets) on its surface.[1–3,8]

Methods to physically or chemically modify the surface of NR to impart hydrophilicity or specific biological recognition groups are of significant interest.[9–19] Notably, there is a need to identify facile methods which create hydrophilic and lubricious properties[20,21] on NR materials to: (1) reduce friction at the NR and tissue interfaces; (2) limit protein adsorption and platelet adhesion to afford non-fouling surfaces[22–25]; and (3) improve the blood-compatibility of NR. These properties will enable NR biomaterials to easily navigate within complex and tortuous anatomical terrains of the body,[23] with the potential to expand the application space of NR in the medical device arena. Effective surface lubrication of guide wires, for example, using hydrophilic polymer coatings results in minimized friction and abrasive forces between the body cavity and device interface.[26] These coatings on guide wires reduce microtrauma within the host environments, thus reducing complications.[27]

A variety of surface polymerization reactions, surface modification techniques, and photo-polymerization reactions have been investigated to prepare NR materials with hydrophilic properties.[1,8,28] Razzak *et al.* grafted N,N-dimethylaminoethylacrylate on NR using a radiation-induced technique with carbon tetrachloride to

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Additional Supporting Information may be found in the online version of this article.
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improve the blood-compatibility and hydrophilicity of NR.[29,30] This grafting technique on NR substrates was reported to be highly dependent on the solvent, monomer concentration, and temperature. UV-induced radical graft polymerization of hydrophilic monomers or low molecular weight macromers, (e.g., methacrylated poly(ethylene glycol), N-vinyl pyrrolidone, 2-methacryloyloxyethyl phosphorylcholine [pMPC],[25] poly(ethylene glycol) [PEG], polyetheyleneoxide, and polyacrylamide), on NR films was also investigated using benzophenone (BP) as the photoinitiator.[8,21] Similarly, the grafting yields for these methods were sensitive to the reaction time and monomer concentration. Pretreatment of NR surfaces with argon plasma[1] improved grafting yields. However, as this deteriorates NR, milder approaches to modify NR are of interest.

Alternative radical polymerization techniques have been explored for grafting hydrophilic monomers containing vinyl groups on NR materials.[2,3] Only a limited number of monomer types were available to undergo these particular reactions. As these radical polymerization reactions were typically performed under stringent conditions, such as elevated temperatures, the initiators, (e.g., peroxides) must be carefully selected to prevent oxidative degradation of the NR material. To address this obstacle, stabilizers or antioxidants were used to scavenge excess free radicals on the NR surface.[31]

In contrast to the approaches above, we are investigating macromolecular photoinitiators composed of hydrophilic and BP units, where the macromolecular photoinitiator performs several functions including: (1) undergoing a free-radical crosslinking reaction with the NR surface on UV irradiation of the BP units; (2) imparting hydrophilicity and lubricity to the NR surface; and, (3) forming an interpenetrating network in the presence of a second hydrophilic polymer.[32] Unlike small-molecule photoinitiators or the combined use of BP and hydrophilic polymers, we hypothesize that hydrophilic high molecular weight macromolecular photoinitiators will provide multiple reaction sites to crosslink with the NR substrate via a multivalent attachment effect (Figure 1). This approach is complementary to those that explored grafting from NR via attachment of an N,N-dialkyldithiocarbamate initiating species and subsequent polymerization of an acrylate,[2,3] or those that investigated immobilizing BP onto a modified glass surface via silane chemistry with subsequent photo-crosslinking of an added polymer.[33–36]
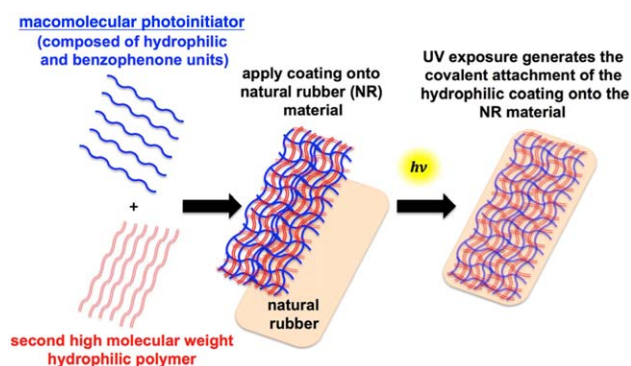

Figure 1. Schematic showing the application of the hydrophilic coating to NR using light, a macromolecular photoinitiator, and a second hydrophilic polymer. The macromolecular photoinitiator and hydrophilic polymer are dissolved in solution and applied to the NR surface as a thin layer. The sample is immediately exposed to a UV light source and washed prior to assessment. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

To determine which macromolecular photoinitiators afford robust hydrophilic coatings on NR surfaces, five macromolecular photoinitiators (Chart 1) were synthesized, possessing BP with various hydrophilic units. We evaluated the effect of monomer molecular weight (2-hydroxyethyl acrylate [HEA] vs. PEG), rigid cyclic vs. non-rigid structures (N-vinylpyrrolidone [NVP] vs. HEA), and charge (acrylic acid [AA]). The introduction of a second high molecular weight hydrophilic polymer (e.g., polyvinylpyrrolidone) [PVP], PEG, or pMPC) was also explored to further enhance the hydrophilicity of the coating. We hypothesized that upon UV irradiation, the second hydrophilic polymer would entangle with the macromolecular photoinitiators, resulting in its entrapment on the NR surface and formation of an interpenetrating network.

Specifically, we report the: (1) synthesis of five macromolecular photoinitiators; (2) identification of the HEA/BP, NVP/BP, and AA/BP macromolecular photoinitiators suitable to form hydrophilic coatings on NR; (3) characterization of these three coatings via FT-IR spectroscopy, contact angle analyses, scanning electron microscopy (SEM), and atomic force microscopy (AFM); (4) coating application optimization with varying formulations and UV exposure times; (5) enhancement of the
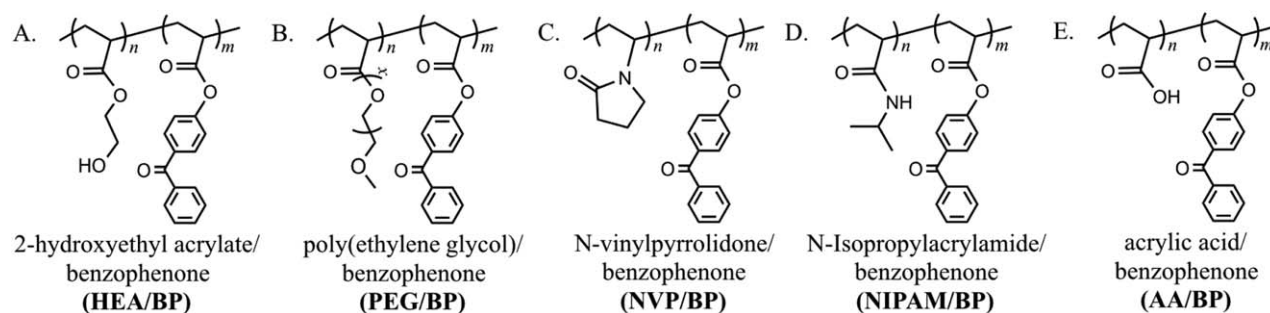

Chart 1. The compositions of the macromolecular photoinitiators investigated for the application of hydrophilic coatings on NR materials. All macromolecular photoinitiators are random copolymers composed of hydrophilic and BP units, which serve as the photoinitiator units for the free radical polymerization reaction when exposed to UV light. n and m refer to the molar ratio of hydrophilic to BP units, respectively. x refers to the number of repeating units of ethylene glycol along the PEG chain in the PEG/BP macromolecular photoinitiator.
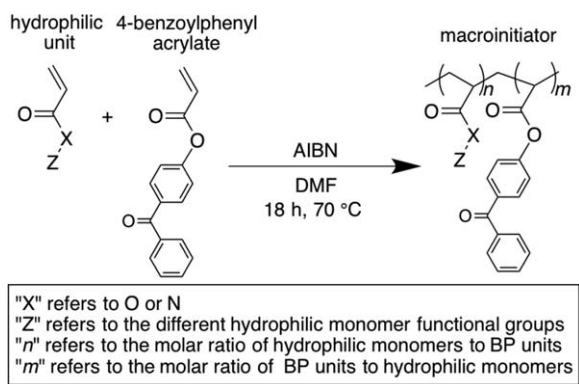
Scheme 1. Synthesis of the macromolecular photoinitiators.

coating's hydrophilicity due to addition of a second high molecular weight hydrophilic polymer; and (6) cytocompatibility of coated NR sheets using an *in vitro* assay.

EXPERIMENTAL

Complete details of the synthesis and characterization of the macromolecular photoinitiators and the methods for characterization of the coatings on NR are found in the Supporting Information.

RESULTS AND DISCUSSION

Macromolecular Photoinitiator Synthesis and Peformance Screening Assays

Synthesis of Macromolecular Photoinitiators. Macromolecular photoinitiators were synthesized using a free radical polymerization reaction with five different hydrophilic acrylate-based monomers[37–48] and 4-benzoylphenyl acrylate, as described in Scheme 1 and listed in Chart 1, using 2,2′-azobis(isobutyronitrile) as the radical initiator.[37–48] Each macromolecular photoinitiator was composed of a randomized copolymer containing ∼10% w/w BP to hydrophilic units at a targeted molecular weight of 100k. A 10% w/w ratio was initially selected as we hypothesized that a greater number of hydrophilic monomers present in the backbone of the macromolecular photoinitiator would afford a water-soluble macromolecular photoinitiator since BP is water-insoluble. This was a critical feature when designing the macromolecular photoinitiator series as NR is not compatible with most organic nonpolar solvents (e.g., benzene, toluene, hexane, and pentane), which results in swelling and deterioration of NR.[49,50]

Following the polymerization reactions, the polymers were purified via dialysis against water and lyophilized to afford white powered solids. The percentage of BP units within each macromolecular photoinitiator was confirmed via ^{1}H-NMR analysis based on the integration of the proton peak from the aromatic protons at $\delta = 7.2–8.0$ ppm (corresponding to BP), which was referenced against protons from the polymer backbone (Table I; see Supporting Information for NMR spectra). All reactions afforded moderate to good yields ranging from 44-96%. Macromolecular photoinitiator molecular weights were measured via GPC and reported in Table I. Macromolecular photoinitiators containing 40% w/w ratio of BP to hydrophilic units were also

synthesized, but these polymers exhibited notably poorer aqueous solubility. Thus, for the next series of experiments, copolymers possessing 10% w/w BP units were investigated.

Initial Screening Assays to Identify Macromolecular Photoinitiators. A screening assay was first performed to identify which macromolecular photoinitiators (Chart 1) created robust hydrophilic coatings on NR sheets. The coating composed of the HEA/BP macromolecular photoinitiator was first investigated with solutions prepared at 1, 2, 5, 10, and 20% w/v concentrations in a 1:1 water and ethanol solution. A thin layer of the polymer solution was applied using a pipette to evenly coat the surface of a 3 × 5 inch NR sheet that was previously washed with water and ethanol, dried under a constant air flow at room temperature, and placed on a glass slide. Samples were then exposed to a UV lamp at 365 nm for 30 min to initiate the free radical polymerization.[1] The absorption of energy excites the BP units to a triplet state, resulting in the abstraction of hydrogen atoms from hydrogen donors along the NR surface and the hydrophilic units.[8,35,51] This abstraction, in addition to the subsequent generation of free radicals, initiates the covalent attachment of the macromolecular photoinitiator to the NR surface.[52–54] Examples of potential mechanisms by which the free radical polymerization reaction can afford covalent attachment of the HEA/BP macromolecular photoinitiator to the NR surface are shown in Figure 2.

The HEA/BP coatings prepared from 5, 10, and 20% w/v solutions resulted in visible, glossy coatings. However, solutions prepared at lower concentrations, 1 and 2% w/v, did not generate detectable coatings. Based on these preliminary observations and for the purpose of this initial screening assay, the remaining coating application experiments were conducted with macromolecular photoinitiators (Chart 1) at a 10% w/v concentration.

All macromolecular photoinitiators listed in Chart 1 were water soluble except for the NVP/BP macromolecular photoinitiator, which was soluble in DMF. To improve its water solubility, the NVP/BP macromolecular photoinitiator was resynthesized with

Table I. Macromolecular Photoinitiator Synthesis Yields and Molecular Weights

Macromolecular photoinitiators	Weight % of BP in macromolecular photoinitiators[a]	Yield (%)	M_n[b]
HEA/BP	10.3	90	129k
PEG (M_n 480)/BP	13.5	44	72.5k
NVP/BP	11.6	96	116k
NIPAM/BP	10.8	77	111k
AA/BP	9.7	83	84.9k

[a] The w/w % BP to hydrophilic units (theoretical weight of 10% w/w) was calculated via NMR integration of the proton peak from aromatic protons from the BP units, which was referenced against protons from the polymer backbone.
[b] All macromolecular photoinitiator were originally synthesized at $M_{w(THEO)}$ of 100k. M_n was determined via GPC analysis in DMF against polystyrene standards or acrylic acid standards for the AA/BP macromolecular photoinitiator.

3% w/w BP instead of 10% w/w to increase the presence of hydrophilic units within the copolymer. Although the modification slightly improved its water solubility, aggregates were still observed in aqueous solution. Thus, the 10% w/w NVP/BP macromolecular photoinitiator was dissolved in a DMF solution, instead of a water/ethanol solution, to prepare the coating on NR.

Each of the five macromolecular photoinitiators were dissolved at 10% w/v concentration and used to coat NR sheets in the same manner as previously described.[35,51–54] After UV exposure, coated NR samples were submerged in a 1:1 water and ethanol mixture for 15 min with stirring to wash unreacted material from the coating and to test whether the coating remained on the NR sheet after the washes. Samples were then placed under a constant airflow at room temperature overnight to dry before analyzing the coating. A control coating application was performed with the HEA/BP macromolecular photoinitiator where the above procedure was followed except without UV light exposure.

Assessment of a coating on the NR sheets was performed using three independent qualitative approaches (Table II). First, coated NR samples were examined for the presence of a thin, glossy coating on the surface. Second, coated NR samples were rubbed back and forth under distilled water (~15–20 rubs) with a human index finger to qualitatively evaluate whether the NR surface was lubricious compared to non-coated NR samples and if the coating remained on the NR sheet after subjection to rubbing. Third, FT-IR spectroscopy was used to detect the coating on the NR surface by identifying chemical features that correlated to the macromolecular photoinitiator structure.[55]

NR sheets coated with the HEA/BP macromolecular photoinitiator resulted in a glossy smooth thin coating that endured the washing in water and ethanol, as well as the index finger rubbing experiments in distilled water. This coating appeared more slippery to the touch, in the presence of water, compared to non-coated NR sheets. FT-IR analysis of the coating showed an absorption band at ~1731 cm^{-1} correlating to the C=O stretch within the HEA structure, as noted in Figure 3, indicating the presence of the HEA/BP macromolecular photoinitiator on the NR surface. UV irradiation of the macromolecular photoinitiator was required to form the hydrophilic coating, as repeating the application procedure without UV exposure did not afford a
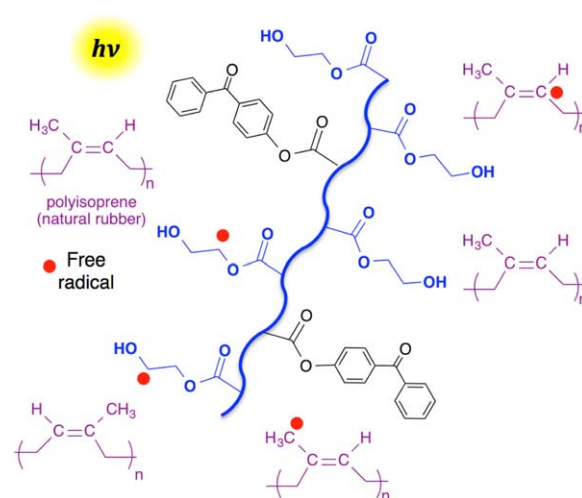

Figure 2. Schematic depicting the proposed mechanisms for the UV-induced covalent attachment of the macromolecular photoinitiator to NR materials using the HEA/BP macromolecular photoinitiator as an example. When the macromolecular photoinitiator is applied on the NR surface and exposed to UV light, free radicals are generated from the BP units. These free radicals abstract hydrogen atoms either from the hydrophilic units along the macromolecular photoinitiators chain, the C=C groups, or unsaturated hydrocarbon groups on NR leading to the covalent attachment of the macromolecular photoinitiator on the NR surfaces. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

coating. Similar glossy and lubricious coatings also resulted with NR samples coated with the NVP/BP and the AA/BP macromolecular photoinitiators (Supporting Information Figure S1). These coatings were measured using a digital micrometer to have a similar average thickness of 7.6 ± 0.4 µm ($n = 10$), which is relatively thin compared to the non-coated NR sheets which had a thickness of about 700 µm.

In contrast, a coating was not evident neither visually nor via FT-IR analysis for the PEG (M_n 480)/BP macromolecular photoinitiator coated NR sheets. On further examination, solutions containing the PEG/BP macromolecular photoinitiator scattered red laser light, consistent with aggregates present in solution. Upon UV exposure, the free radicals generated on the backbone of the macromolecular photoinitiator are shielded by the

Table II. Qualitative Assessments of NR Hydrophilic Coatings

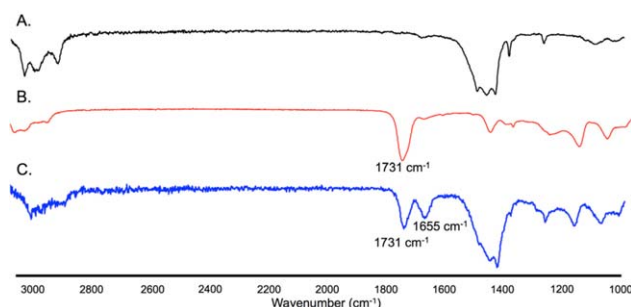| Hydrophilic coatings on NR sheets	Qualitative assessments		
	Glossy coating on the NR	Lubricious compared to uncoated NR	Remains after rubbing with water
HEA/BP	Yes	Yes	Yes
HEA/BP (no UV exposure)	No	No	No
PEG/BP	No	No	No
NVP/BP	Yes	Yes	Yes
NIPAM/BP	No	No	No
AA/BP	Yes	Yes	Yes

Figure 3. FT-IR spectra of (A) non-coated NR sheet; (B) NR sheet coated with a 5% w/v solution of the HEA/BP macromolecular photoinitiator with a resulting peak at 1731 cm^{-1}; and (C) NR sheet coated with a 5% w/v solution of the HEA/BP macromolecular photoinitiator and 2% w/v of PVP with resulting peaks at 1731 and 1655 cm^{-1}. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

aggregate preventing a reaction with the NR substrate and formation of a coating.

This coating application was reattempted by extending the UV exposure from 30 to 60 min. As a coating was still undetectable, the PEG/BP macromolecular photoinitiator was not further studied. Likewise, the NIPAM/BP macromolecular photoinitiator coating application also resulted in an undetectable coating on the NR sheets after the washes. Neither extending the UV exposure time nor increasing the macromolecular photoinitiator concentration resulted in a durable coating. As the NIPAM/BP macromolecular photoinitiator in solution also scattered red laser light, it is likely that aggregates prevented the macromolecular photoinitiator from covalently attaching to the NR surface. Thus, the NIPAM/BP macromolecular photoinitiator was not further evaluated.

Hydrophilic Coating Application Assessment. Based on the UV irradiation coating mechanism, the presence of the unsaturated C=C bonds in NR was necessary to generate the hydrophilic coating (Figure 2). Therefore, this coating application procedure was repeated using the 10% w/v HEA/BP macromolecular photoinitiator solution on nitrile (a copolymer of acrylonitrile and butadiene) and neoprene synthetic rubber (repeating units of chloroprene) substrates, which also possess unsaturated C=C bonds. The coating was applied on these surfaces in a similar manner as described previously, which resulted in a visible coating that was slippery via touch in the presence of water. This finding strengthened the proposal that C=C bonds present on the substrate were necessary for forming the coating. To further confirm this, the coating application was repeated with substrates lacking unsaturated C=C bonds, such as borosilicate glass, polyethylene, and polyurethane. Coatings were not detectable on these materials, which verified the critical role of these chemical features in the formation of hydrophilic coatings on NR (Figure 2).

A reported alternative method to prepared NR coatings involved a photo-induced graft polymerization reaction using BP as the photoinitiator. For these reactions, the NR substrates were soaked in an ethanol solution of BP prior to photo-polymerizaton.[8,56] Thus, we investigated whether soaking NR sheets in a

BP solution prior to grafting poly(acrylic acid) (M_n 20,000) (pAA) created a similar hydrophilic coating compared to the one formed using the AA/BP macromolecular photoinitiator. For these studies, NR sheets were soaked in ethanol containing BP at 0.1, 1, or 5% w/v for 1 or 2 h. As a control, NR sheets were soaked in a solution with the AA/BP macromolecular photoinitiator at similar concentrations. The NR sheets were removed from solution, dried, placed on glass slides, and a thin layer of a 5 w/v % pAA solution was applied on the surface of the BP treated NR sample. All samples were exposed to 30 min of UV light, washed in ethanol and water in a similar manner as previously described, and dried under a constant air flow at room temperature overnight. NR sheets soaked in the BP solutions followed by treatment with pAA and UV light were not hydrophilic, lost their elasticity, became brittle, and easily broke when stretched. In contrast, samples treated with the AA/BP macromolecular photoinitiator gave a hydrophilic coating on NR, as described above. These findings underscored the importance of incorporating the BP moiety into a macromolecular photoinitiator, to eliminate the small molecule's damaging effects on NR elasticity.

Macromolecular Photoinitiator Solution Concentration Variation. As the HEA/BP, NVP/BP, and AA/BP macromolecular photoinitiator met the initial criteria from the above screening assays, their resulting coatings were further characterized. Contact angle measurements, were conducted on coated NR samples prepared from the HEA/BP, NVP/BP, or AA/BP macromolecular photoinitiator. The average contact angle measured for the surface of the non-coated NR was 117.2° ± 5.6° ($N = 5$). When NR samples were coated with the 10% w/v HEA/BP, NVP/BP, or AA/BP macromolecular photoinitiator, and exposed to UV light for 30 min, contact angles notably decreased approximately 30° (Table III), indicating a more hydrophilic surface compared to non-coated NR sheets. The coating application using 5 and 2% w/v macromolecular photoinitiator solutions was also explored to determine the relationship between contact angle measurements and macromolecular photoinitiator concentration. Decreasing the macromolecular photoinitiator concentration from 10 to 2% w/v resulted in increased contact angle values for all three macromolecular photoinitiators, with similar values to that of non-coated NR sheets. For all three macromolecular photoinitiator, similar contact angle values were found for the 2, 5, and 10% w/v concentration groups,

Table III. Contact Angle Measurements of NR Sheets Coated with Varying Concentrations of the Macromolecular Photoinitiator

Initiator	Solution concentration		
	10% w/v[a]	5% w/v[a]	2% w/v[a]
HEA/BP	88.6 ± 1.3	91.5 ± 7.1	100.8 ± 4.7
NVP/BP	87.0 ± 4.3	83.4 ± 13.9	99.5 ± 6.0
AA/BP	83.4 ± 13.9	87.1 ± 2.8	94.4 ± 11.1

[a] Contact angle measurements were obtained at an $N = 5$ and reported in degrees.

independent of the macromolecular photoinitiator used for the coating application.

Introduction of Second High Molecular Weight Synthetic Hydrophilic Polymers

To further enhance the hydrophilicity of the coating, we explored the addition of a second high molecular weight synthetic hydrophilic polymer to the coating such as PVP,[26,57] PEG,[22] or pMPC.[25] These polymers contain a high number of repeated polar or charged functional groups along their polymer backbone. PVP is used in many applications due to its extremely low cytotoxicity, non-antigenicity, and high water-solublily.[58] PEG is compatible with aqueous photo-curing systems[55] and can be grafted onto surfaces of biomedical devices to improve their biocompatibility and reduce thrombogenicity.[59] pMPC, composed of units bearing a phosphorylcholine group, is highly water soluble and biocompatible. Surfaces modified with pMPC can afford low friction and anti-biofouling properties,[25,60] and hence, it is widely used for a variety of surface fouling challenges in medical device applications.

These hydrophilic polymers were incorporated into the coating by dissolving them in solution at 2% w/v along with a macromolecular photoinitiator at 5% w/v. The coating was applied and characterized as previously described. The FT-IR spectrum of the NR samples coated with 5% w/v HEA/BP and 2% w/v PVP (M_n 360k) showed distinct absorption bands at 1731 cm^{-1} and at 1655 cm^{-1} for the C=O stretch of the HEA/BP macromolecular photoinitiator and of PVP, respectively (Figure 3). The introduction of PVP to the coating resulted in a further decreased contact angle value from 83.4 ± 13.9 to $84.8° \pm 5.6°$ (Table IV), indicating that the addition of PVP enhanced the hydrophilicity of the coating. These studies were repeated with PEG and pMPC. The addition of 2% w/v PEG (M_n 20k) resulted in a decreased contact angle of $74.8° \pm 2.4°$, while the addition of 2% w/v pMPC (MW$_{THEO}$ 100k) afforded the smallest contact angle of $27.4° \pm 5.8°$ (Table IV). FT-IR spectra of the coatings composed of the HEA/BP macromolecular photoinitiator with either PEG or pMPC are shown in Supporting Information Figure S2. For the NVP/BP macromolecular photoinitiator, the addition of PVP resulted in a decreased contact angle value from 91.5 ± 7.1 to $73.2° \pm 7.5°$. pMPC was not studied with the NVP/BP macromolecular photoinitiator due to its limited solubility in DMF. Repeating the study with the AA/BP macromolecular photoinitiator gave similar results to those observed with the HEA/BP and NVP/BP macromolecular photoinitiators, in that the addition of the hydrophilic polymer to the coating decreased the contact angle value. However, a greater magnitude of contact angle change was observed. For example, the addition of PVP to the coating resulted in a decreased contact angle value from 87.1 ± 2.8 to $32.8° \pm 8.8°$. Similarly, the addition of PEG or pMPC decreased the contact angle value to 29.9 ± 7.4 and $23.6° \pm 5.7°$, respectively. To investigate the necessity of the macromolecular photoinitiator, in the presence of the second hydrophilic polymer to form the coating, the above experiment was repeated with the 2% w/v PVP without the HEA/BP macromolecular photoinitiator. A coating was neither detectable visually nor via FT-IR analysis; confirming that on UV exposure, the macromolecular photoinitiator is

Table IV. Contact Angle Measurements of the Coated NR Samples with the Addition of a Second Hydrophilic Polymer

Hydrophilic polymer	Macromolecular photoinitiators		
	HEA/BP[a]	NVP/BP[a]	AA/BP[a]
No polymer	91.5 ± 7.1	83.4 ± 13.9	87.1 ± 2.8
PVP	84.8 ± 5.6	73.2 ± 7.5	32.8 ± 8.8
PEG	74.8 ± 2.4	76.3 ± 1.8	29.9 ± 7.4
pMPC	27.4 ± 5.8	[b]	23.6 ± 5.7

[a] Contact angle measurements were obtained at an $N = 5$ and reported in degrees. PEG used for these experiments had an M_n of 20,000. All macroinitiators were prepared at 5% w/v with or without 2% w/v of the hydrophilic polymer.
[b] The coating contact angles of NVP/BP with pMPC were not measured due to insolubility of the hydrophilic polymer in DMF.

necessary to induce the crosslinking with the NR substrate and to entrap the second hydrophilic polymer on the surface.

Advancing and receding contact angle measurements were compared between the non-coated and coated NR samples with the HEA/BP, NVP/BP, or AA/BP macromolecular photoinitiator at 5% w/v with 2% w/v PVP, as noted in Supporting Information Table S1, to compare their wetting properties. The contact angle hysteresis was noted for each sample by the difference between the advancing and receding contact angle values for each sample. NR samples coated with the AA/BP macromolecular photoinitiator and PVP showed the lowest hysteresis (6.1°), indicating a greater ability to wet the surface, while non-coated NR samples showed the greatest hysteresis (76.4°).

Effects of Varying Macromolecular Photoinitiator Molecular Weight and BP Content

Each macromolecular photoinitiator was synthesized at three different molecular weights (MW; g/mol): 31k, 42k, and 129k for the HEA/BP macromolecular photoinitiator; 44k, 78k, and 132k for the NVP/BP macromolecular photoinitiator; and finally, 24k, 44k, and 244k for the AA/BP macromolecular photoinitiator, to investigate the effects of macromolecular photoinitiator MW on the hydrophilic coating properties. All macromolecular photoinitiators were composed of 6% w/w BP to hydrophilic units and GPC was conducted to verify the different MWs for each copolymer (Supporting Information Table S2). Solutions of the three macromolecular photoinitiators at these different molecular weights were prepared at 5% w/v and applied onto the NR sheets in a similar manner as previously described. Coatings were detectable, both visually and by FT-IR analysis, for all nine samples and resulted in similar qualitative observations as noted in Table II. Contact angle analysis indicated that varying the macromolecular photoinitiator MW or decreasing the ratio of BP to hydrophilic units from 10 to 6% w/w did not significantly affect contact angle measurements or the ability of the coating to remain on NR sheets after the washes.

Optimization of UV Exposure Time for Coating Application

We next determined whether UV exposure periods of less than 30 min induced the free radical polymerization reaction of the
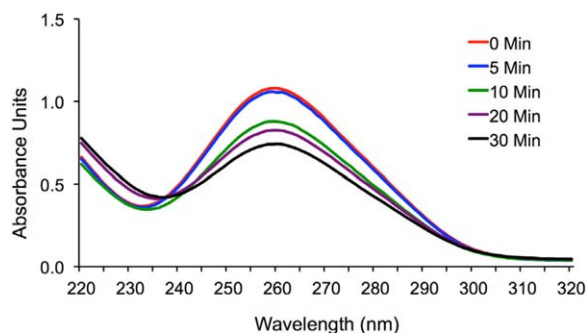
Figure 4. UV/Vis spectra of the HEA/BP macromolecular photoinitiator as a function of UV exposure time. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

macromolecular photoinitiator. For these studies, UV/Vis spectroscopy was used to monitor the reaction at 5, 10, 20, and 30 min of UV exposure.[61,62] For the HEA/BP macromolecular photoinitiator, the absorption signal at 261 nm gradually decreased with increasing UV exposure time, indicating the continual consumption of BP units during photolysis (Figure 4), as the local minima at approximately 230 nm shifted to longer wavelengths with increasing UV exposure. A similar trend was also observed for the AA/BP macromolecular photoinitiator under these conditions (Supporting Information Figure S3). Due to the interfering background absorption from the DMF solvent, the NVP/BP macromolecular photoinitiator was unobservable.

These results suggested that a minimum of 10 min of UV exposure was required to initiate the photolysis of the BP units within the macromolecular photoinitiator. Thus, fewer minutes of UV exposure than 30 min were used to prepare the hydrophilic coating on NR sheets. A solution of the 5% w/v HEA/BP macromolecular photoinitiator with 2% w/v PVP was applied onto NR sheets which were exposed to 0, 1, 5, 10, or 30 min of UV light, washed, and assessed as previously described. As noted in Table V, coated NR samples exposed to 0 or 1 min of UV light resulted in contact angle measurements similar to non-coated NR samples, indicating that the coating was not present as a result of insufficient UV exposure. Longer UV exposure times of 5, 10, and 30 min resulted in hydrophilic coatings on the NR surface with comparable contact angle values. Based on these results, SEM and AFM, as well as cytotoxicity experiments were conducted with the coated NR samples fabricated using 10 min of UV light exposure.

Table V. Contact Angle Measurements of the Coated NR Samples with the HEA/BP Macromolecular Photoinitiator (5% w/v) and PVP (2% w/v) with Varying UV Exposure Time

UV exposure time (min)	Contact angle (°)
0	113.0 ± 3.3
1	116.4 ± 6.7
5	89.3 ± 7.7
10	80.8 ± 2.8
30	84.8 ± 5.6

N = 5.

SEM Characterization of the Coated NR Surfaces

SEM images were obtained of coated and non-coated NR sheets to compare the topology of the coatings. Coated NR samples were prepared using the 5% w/v macromolecular photoinitiator (either HEA/BP, NVP/BP, or AA/BP) with or without 2% w/v PVP, and 10 min of UV light exposure. The SEM image of a non-coated NR sample [Figure 5(A)] showed surface irregularities and roughness with features on the micron scale. SEM images of the coated NR samples [Figure 5(B–D)] revealed a more homogenous and smoother surface compared to the non-coated NR sample.

AFM Characterization of Surface Topology, Roughness, and Friction

AFM was performed on the NR samples to compare the surface topology, roughness, and friction. Non-coated and coated NR sheets were prepared with 5% w/v HEA/BP, NVP/BP, or the AA/BP macromolecular photoinitiator with 2% w/v PVP. Three-dimensional AFM images of the topography were obtained of the non-coated and coated NR sheets in air (Figure 6; enlarged images shown in Supporting Information Figure S4). The surface of non-coated NR samples [Figure 6(A)] exhibited submicron roughness with an rms value of 275 ± 31 nm. In contrast, AFM images of coated NR samples depicted different nano-topological profiles with smoother surfaces, consistent with the SEM data (Figure 5). NR sheets coated with either the HEA/BP macromolecular photoinitiator and PVP [Figure 6(B)] or AA/BP macromolecular photoinitiator and PVP [Figure 6(D)] depicted a smooth and homogenous surface with rms values of 8.2 ± 1.5 nm and 3.1 ± 0.5 nm, respectively. However, a greater roughness value with a rms of 168 ± 62 nm was obtained for the NVP/BP and PVP coated NR sheet. This is due to the presence of several uncoated patches from the heterogeneous latex surface, as noted by the darker spots in the AFM image [Figure 6(C)].

We hypothesized that the coating application on NR sheets from all three macromolecular photoinitiator with PVP formed a covalently attached coating capable of covering the irregularities on the NR surface which resulted in a smoother and homogenous surface. Studies have been conducted to understand the influence of surface roughness on wettability. Miller et al.'s analysis using AFM and contact angle analysis goniometry indicated that rougher surfaces led to a greater difference between advancing and receding contact angles, resulting in decreased wettability properties on rough and smooth polytetrafluorethylene films.[63] Similar findings of decreased wettability on rougher surfaces were reported by Busscher et al.[64] and Hitchcock et al.[65] These results reflected our findings in which non-coated, rough NR surfaces have greater contact angle hysteresis and poorer wettability while smoother, coated NR surfaces showed lower contact angle hysteresis with improved wettability (Supporting Information Table S1). Thus, we posit that the coating application resulted in a more hydrophilic surface on NR sheets due to the hydrophilic components in the coating in addition to the smoother topological surface.

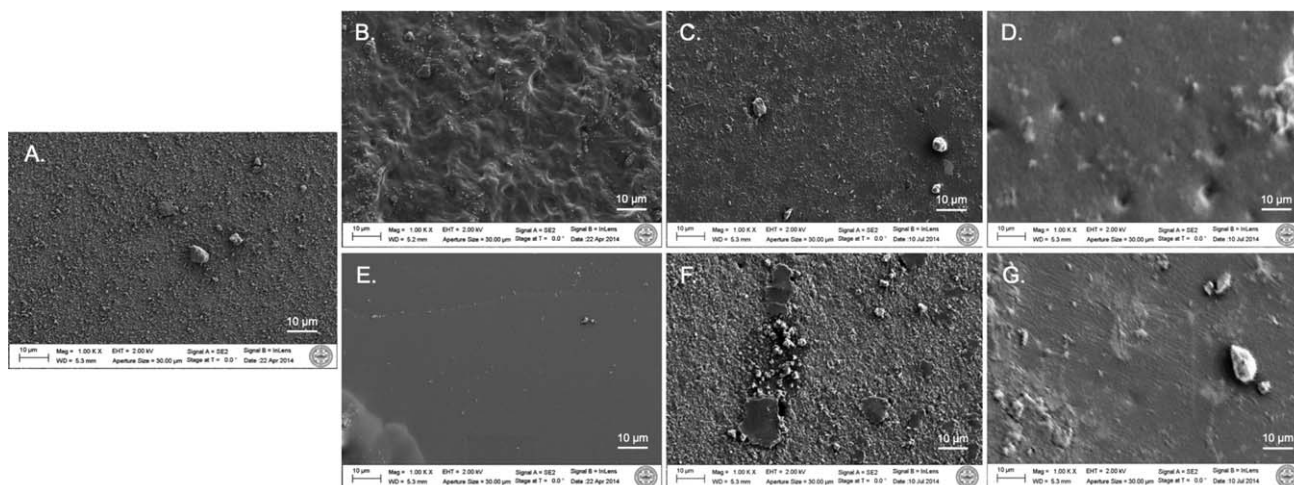To compare the friction coefficients between non-coated and coated NR samples (5% w/v HEA/BP macromolecular

Figure 5. SEM images of the NR samples with or without the hydrophilic coating. (A) non-coated NR control; (B) NR sample coated with the HEA/BP macromolecular photoinitiator; (C) NR sample coated with the NVP/BP macromolecular photoinitiator; (D) NR sample coated with the AA/BP macromolecular photoinitiator; (E) NR sample coated with the HEA/BP macromolecular photoinitiator and PVP; (F) NR sample coated with the NVP/BP macromolecular photoinitiator and PVP; (G) NR sample coated with the AA/BP macromolecular photoinitiator and PVP. Solutions for the coatings were prepared at 5% w/v macromolecular photoinitiator with or without 2% w/v PVP, and with 10 min of UV exposure. Scale bars, 10 μm.
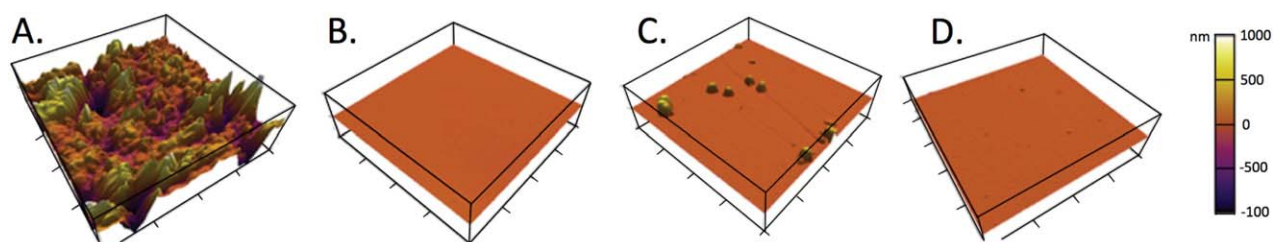

Figure 6. AFM images depicting the topography and roughness of NR samples coated with or without the hydrophilic coating. (A) non-coated NR control; (B) latex sample coated with the HEA/BP macromolecular photoinitiator at 5 and 2% w/v of PVP; (C) NR sample coated with the NVP/BP macromolecular photoinitiator at 5 and 2% w/v of PVP; and (D) and NR sample coated with the AA/BP macromolecular photoinitiator at 5 and 2% w/v of PVP. $N = 4$. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

photoinitiator, NVP/BP macromolecular photoinitiator, or AA/BP macromolecular photoinitiator with 2% w/v PVP), lateral force microscopy was conducted to obtain lateral force profiles. The normal force was determined by the sum of the normal load and adhesion forces from normal force spectroscopy.[66] In all cases, non-coated and coated NR samples showed relatively high frictional force, even in excess of the normal load which is typically observed in AFM studies under low-load frictional conditions where intermolecular adhesion forces exceed the external normal load.[67] However, when repeating this frictional study after submerging the NR samples in water for 15 min, the frictional force for all three coated NR samples significantly decreased. The non-coated NR samples in water showed the greatest friction coefficient value of 0.94 ± 0.18, whereas the HEA/BP and PVP coated NR samples exhibited a superior frictionless surface with a friction coefficient value of 0.03 ± 0.02 (Table VI). The NVP/BP and PVP and AA/BP and PVP coated NR samples exhibited friction coefficients of 0.19 ± 0.06 and 0.30 ± 0.23, respectively. Results from the frictional analysis showed that all three hydrophilic macromolecular photoinitiator coatings reduced the friction on NR surfaces in the presence of water.

Coating Cytotoxicity against NIH 3T3 Fibroblasts

Finally, a colorimetric cell-viability assay was performed using NIH 3T3 fibroblast cells (ATCC) to investigate cytotoxic effects arising from potential leachables from the hydrophilic coating on the NR sheets. A transwell cytotoxicity assay was selected for this investigation, as this experiment is part of the FDA-required experiments for medical device development (ISO

Table VI. AFM Friction Coefficient Values for the Non-Coated and Coated NR Samples Conducted in Air and after Being Submerged in Water

Natural rubber samples	Friction coefficient[a] (in air)	Friction coefficient[b] (in water)
Non-coated	2.87	0.94 ± 0.18
HEA/BP and PVP	0.06	0.03 ± 0.02
NVP/BP and PVP	1.90	0.19 ± 0.06
AA/BP and PVP	4.22	0.30 ± 0.23

[a] $N = 1$ was conducted for samples conducted in air.
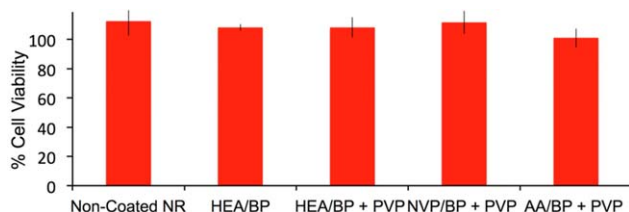[b] $N = 3$ was conducted for samples conducted in water.

Figure 7. Results from transwell cell viability assay of coated and non-coated NR samples (5% w/v HEA/BP, NVP/BP, and AA/BP macromolecular photoinitiator with or without 2% w/v PVP) using an MTS assay. $N = 3$. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

10993). NR samples were coated with the 5% w/v HEA/BP, NVP/BP, or AA/BP macromolecular photoinitiator with or without 2% w/v PVP, exposed to 10 min of UV exposure, cut into 2 × 1 inch pieces, washed with ethanol, dried, and transferred into transwell plates. An *in vitro* cell viability assay was performed using a standard MTS proliferation assay protocol.[68] As shown in Figure 7, coated NR samples did not induce any notable cytotoxic effects, as the results were similar to uncoated controls after a 4-h incubation.

CONCLUSIONS

NR is a key component of many products due to its favorable properties, renewable source, and low cost. Thus, research to further understand the chemical reactivity and properties of NR and strategies to modify its chemical, physical, and mechanical properties are and will continue to be an active area of interest. In this report, three macromolecular photoinitiators (HEA/BP, NVP/BP, and AA/BP) are synthesized and characterized. Use of these macromolecular photoinitiators and a facile UV light photo-chemical procedure introduces a hydrophilic and lubricious coating on NR surfaces. An optimized coating formulation and application procedure are described after varying the macromolecular photoinitiator molecular weights, solution concentrations, and UV exposure times. The resulting coated NR sheets appear smooth and glossy and are lubricious in the presence of water. FT-IR spectroscopy verifies the presence of the coating, and contact angle measurements reveal the coated NR samples to possess a more hydrophilic surface compared to non-coated NR samples. The hydrophilicity of the coating is further enhanced by the addition of a second hydrophilic polymer (PVP, PEG, or pMPC) to the coating. SEM analysis shows the coating to be homogenous and smoother than non-coated NR samples. Atomic force frictional studies document the reduced friction of the coated NR samples compared to the non-coated NR samples in the presence of water. These coated NR samples are non-cytotoxic. The presence of BP in the macromolecular photoinitiator is key for preparation of the hydrophilic coating, as in the presence of UV light a chemical crosslinking reaction occurs with the NR. Without exposure to light or use of HEA, NVP, and AA polymers alone does not afford a hydrophilic coating. Moreover, the use of BP itself results in a loss of NR elasticity and becomes brittle, thus underscoring the importance of incorporating the BP moiety into the macromolecular photoinitiator. Initial studies also show that the coating process is transferrable to other

substrates possessing unsaturated double bonds such as nitrile and neoprene. These findings complement ongoing efforts in the field, and expand the repertoire of coating strategies available for NR. Continued research efforts will afford NR materials with enhanced surface properties for novel applications.

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