ReSettle: an antimicrobial UV-curable nail gel for immunocompromised patients

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Abstract:

The recovery from cancer is a difficult and long process of returning to ‘normal’ life. The positive correlations between self-care and cancer recovery suggest that cosmetic services, such as nail care, support recovery. However, due to the risk of nail infections, it is not safe for an immunocompromised patient to have artificial nails. This paper focuses specifically on chloronychia (GNS), gel nail polish and extensions, and proposes a design to inhibit the growth of GNS-causing *P. aeruginosa.* Silver phosphate glass was the chosen antimicrobial for this concept. It would be integrated into a formula of UDMA, EMA, BAPO, and MEHQ to create a UV-curable gel that exhibits antimicrobial properties. Seven stages were suggested in order to test the feasibility of a UV-curable antimicrobial gel. Ideally, this product would serve as an additional safe nail service option for those in recovery.

Introduction:

Even after cancer treatment, many struggle to return to ‘normal’ and are still left with physical and emotional burdens. For many people in recovery from cancer treatment, self-care is a way to lift the psychological load and support recovery. Studies show that beauty treatments and care have a beneficial impact on those in cancer recovery (30). In this regard, nail services and nail care are a recognized part of returning to normality (21, 31).

During and after cancer treatment, patients are strongly advised not to get their nails done mainly due to the risk of infection. Although doctors consistently recommend avoiding nail services, the timeframe is not mentioned (5, 17) or not specified (6), while nail industry experts typically cite a 3- to 6-month wait after treatment (11). It should be noted that patients on informal online forums typically report waiting several months longer than that period. Hence, there is no measurable indicator for when artificial nails will not pose a risk, so patients are left guessing and feeling uneasy about nail services.

The danger of infection with artificial nails, specifically gel enhancements, is accurately established. Artificial nails can become a breeding ground for dangerous microbes as they create a pocket that traps moisture between the natural and artificial nail. *Pseudomonas aeruginosa* colonizes the nail when overexposed to moisture, causing chloronychia. Also known as green nail syndrome, chloronychia is generally painless and benign in healthy people (33). Conversely, in immunocompromised patients, the risk of *P. aeruginosa* becoming a serious or fatal infection increases immensely (38). Chemotherapy introduces the perfect conditions for such infections to occur through disabling the immune system.

The only method of prevention is avoidance, but that still leaves individuals fearing infection from their nails, as there is no defined clearance date. A solution that minimizes the risk of infection from artificial nails provides an additional option for immunocompromised persons

who want to get their nails done. Antimicrobial UV-cured resins are being formulated in dentistry, but they have not been adapted to nail systems. Hence, such methods were reviewed for this design. This paper proposes testing and experimentation for a UV-curable interface layer incorporating silver phosphate glass particles in order to reduce microbial infection with artificial gel nails.

Figure 1.

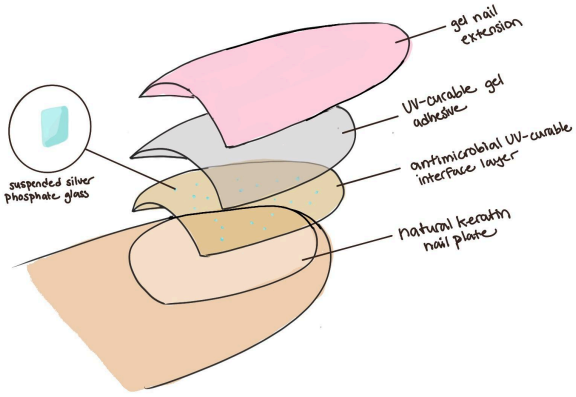


Illustration of ReSettle product within gel nail system (not to scale).

Background

Chemotherapy

Patients undergoing chemotherapy are subject to immune compromise through several simultaneous mechanisms. Chemotherapy targets cancer cells but also normal cells, such as bone marrow cells, resulting in myelosuppression and subsequent neutropenia. Additionally, chemotherapy further increases the risk of severe infections by negatively affecting the abilities of neutrophils. It causes chemotactic and phagocytic defects that impair neutrophils' ability to navigate and engulf microbes (9). Therefore, an immune system can still be impaired despite having a normal cell count.

Finishing cancer treatment does not mean immediate immune recovery, and it is unclear across multiple sources when the immune system returns to being fully capable (5, 17, 6). In a study on the impairment of immune recovery after breast cancer treatment, it was shown that over 12 months, immune measures did not return to pre-treatment baseline levels. The percentages of

patients' immune recovery to baseline or above varied from 6% to 76% among all immune parameters, which reinforces why it is unknown when immune recovery happens (18).

Chloronychia and Artificial Nails

A chloronychia infection, or green nail syndrome (GNS), is found in the nails and characterized as a green discoloration varying from blue-green, green-brown, to green-yellow (33). It is caused by *Pseudomonas aeruginosa,* a Gram-negative bacterium that causes nosocomial infections and fatal infections in the immunocompromised. It also has the ability to form protective biofilms and has high intrinsic antibiotic resistance, making many treatments ineffective, which leads to long-term persistence and increased mortality (38). It is typically present in patients with underlying conditions such as onycholysis, onychotillomania, chronic paronychia, and nail disorders (8). Furthermore, chronic exposure to moisture, water, soap, and detergents is the most common cause of the infection, as described in a study done on patients with discolored nails (7). Hence, workers whose jobs require frequent hand-washing or disposable gloves, like healthcare workers or janitors, are at higher risk of infection (2).

GNS is nearly harmless to the average person but can cause serious damage in immunocompromised individuals. *(38, 33)*. There is a very low risk of GNS becoming systemic in healthy people, but in patients with an impaired immune system, there is a higher risk of secondary infection (2). The pathogen of GNS, *P. aeruginosa,* is recognized as a main cause of severe sepsis and death among neutropenic cancer patients. Furthermore, in recent years, the pathogen has increasingly been reported as a cause of bloodstream infections, which is a significant cause of morbidity and mortality in patients with neutropenia (12).

The infection is usually painless, and patients diagnosed with it usually report no signs of pain, swelling, redness, fever, or chills (4, 33). This can be dangerous for patients who could contract a systemic infection from *P. aeruginosa* because they would only know they have GNS if they see its green indicator. Since artificial nails often cover the nail plate, a carrier wouldn't be able to see that indicator. Additionally, a patient could autologously spread the infection by scratching or rubbing their skin, especially if the skin is damaged (33). This is especially relevant to nail services because of the trimming process many nail technicians use on the cuticle. Therefore, timely treatment may not be delivered, and the infection could worsen.

Artificial nails set up the prime conditions for a chloronychia infection through providing a moisture-trapping pocket for *P. aeruginosa* to colonize. Between the natural nail and the artificial enhancement, microscopic gaps may occur, allowing for water, soap, or detergent to sit directly against the nail plate for prolonged periods of time. The pathogen thrives in moist environments, which artificial nails cultivate. Hence, artificial nails are a known cause of GNS (4). This also suggests that a person does not need to have a job with chronic exposure to water or tight clothing on the hands and feet; daily activities such as washing the dishes or taking a shower can trap water and leave people at high risk of infection.

Artificial nails can cause a nail disease called onycholysis, which is the painless separation of the nail plate from the nail bed. It is often caused by trauma, but it can also be caused by prolonged water exposure or fungal infections (27). Therefore, the micro-pockets that allow water to enter between the natural nail and the gel enhancement can cause onycholysis, which may lead to bacterial infection. Additionally, harsh removal of gel nails, overfiling, and the chemicals in gel nails can cause onycholysis (26). Although it is painless and simple to treat when caused by physical damage, onycholysis provides a space for *P. aeruginosa* to colonize since the pathogen is not part of the normal skin flora (8).

Additionally, there have been documented deaths associated with infected nails coming into contact with patients at high risk of infection. In a study that examined healthcare workers' nails during a *P. aeruginosa* infection outbreak in an infant care hospital, they found evidence that associated the infection with nurses with artificial or long nails. (24). The outbreak resulted in 10.5% of 439 neonates acquiring the infection, with 35% of those dying. It should be emphasized that the patients were infants, who have a different immune system to that of chemotherapy patients, but both are at high risk of severe infection. Furthermore, in another study that analyzed the number of microbes on nurses with artificial nails versus native nails, more pathogens were found in those with artificial nails (13). This strongly suggests artificial nails played a role in the colonization of *P. aeruginosa* on the healthcare workers' nails.

Prevention methods for GNS in people with artificial nails are only avoidance because there is no solution to prevent infections under the enhancement as of now. Using antimicrobial treatments or disinfecting solutions is less effective against *P. aeruginosa,* as suggested in a study that found the use of antimicrobial soap or alcohol-based gel was much less effective in artificial nails than in native nails (22).

Antimicrobial Light-Cured Dental Restorative Materials

Dental restorative materials can be used as a precedent for a solution to the issue of GNS with artificial enhancements. The materials science behind light-cured dental adhesives and gel nails is fundamentally similar. Both are formulated with a polymerizable methacrylate oligomer system and are intended to attach to a substrate while being flexible, optically clear, and durable (29). One of the significant turning points in nail enhancement developments was when dentist Fred Slack used dental acrylate to fix his nail (23). While there is research on antimicrobial dental adhesives, I found that it has not been applied to cosmetics. That said, this provides evidence that antimicrobial agents can be incorporated into a light-cured methacrylate-based polymer while maintaining functional properties.

Silver Phosphate Glass

Silver phosphate glass as the antimicrobial additive is chosen as an effective option against *P. aeruginosa* and the most compatible with this design. In one of the earliest studies done on silver phosphate glass by Valappil et al., it was shown that silver phosphate glass is within the range of reducing *P. aeruginosa* biofilms as well as being safe in terms of cyto-/biocompatibility (42). Furthermore, silver phosphate glass allows for controlled release because the rate of release is based on the degradation of the glass (41). Therefore, the antimicrobial would activate when exposed to moisture, or more specifically for this design: when the nail enhancement lifts. As the glass would be suspended in a cured gel, its ion release mechanism allows for antibacterial activity when moisture gets trapped underneath the artificial nail. Additionally, the rate of dissolution of the glass can be easily manipulated by changing the glass composition (20). For instance, multivalent cations, such as B^{3+} or Fe^{3+}, would decrease the dissolution rate as they would have a positive effect on the durability of the glass. (35). Hence, the composition of the silver phosphate glass can be specific to the 2-4 weeks.

Although silver phosphate glass has shown to have high promise to work well in the interface layer, there are still multiple problems that must be considered. Ionic silver goes through a photoreduction reaction when exposed to light, which makes it appear dark. This is a significant issue as a UV-cured layer needs to be optically clear to be fully cured and safe against gel allergies. Even more critical is that silver ions lose most of their antimicrobial properties when they gain an electron from light exposure. The antimicrobial activity of the silver phosphate glass will depend on whether the silver is present as Ag+ or Ag0, but I could not find material on silver ions staying ions when exposed to UV light. Additionally, random light scattering may occur from a refractive index mismatch between the glass particles and the surrounding matrix (44). Light scattering would result in an opaque material, and refractive index matching can be used to match the index of the methacrylate resin to the glass, which is similar to how dental resins incorporate bioactive glass into light-cured resins. Furthermore, there are certain regulatory restrictions on silver in cosmetics, such as in the EU, where micron-sized silver, when used up to 0.3% in nail products, is considered safe (34).

Design

Hypothesis: An antimicrobial UV-curable nail gel utilizing silver phosphate glass will be effective against *P. aeruginosa* while still being biocompatible and maintaining mechanical properties.

The design of the interface layer must follow specific constraints. It needs to deliver effective antimicrobial activity against *P. aeruginosa* for 2-4 weeks. Also, it needs to have strong adhesion to the keratin nail plate, flexibility, optical clarity, biocompatibility, and appropriate curing for salon UV lamps.

The proposed ingredients that are most likely to produce the desired results are displayed in Table 1.

Table 1.

Type	Ingredient	Function in design
Film-forming oligomer	Diurethane dimethacrylate (UDMA)	Backbone monomer that was tested for compatibility with active agent
Reactive monomer	Ethyl Methacrylate (EMA)	Nail industry standard
Photo initiator	Phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide; BAPO	Deep curing, range of 360-440 nm, Type I photoinitiator
Polymerization inhibitor	4-methoxyphenol (MEHQ)	Shelf stability
Antimicrobial additive	Silver phosphate glass (fine grade, <5 μm)	Antimicrobial activity
Surface treatment	3-methacryloxypropyltrimethoxysilane (MPS)	Chemical coupling between glass and methacrylate prevents

The film-forming oligomer is the matrix or backbone of the light-cured interface layer. Diurethane dimethacrylate was chosen because a study on drug administration through UV-curable nail polish conducted testing that showed these materials can cure under UV in 2 minutes while holding an active agent. Along with that, the reactive monomer, EMA, was also used in the Kerai et al. (2015) study (19).

Phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide, or BAPO, is a possible photoinitiator. Although the study incorporating a drug into artificial nails used 2-hydroxy-2-methylpropiophenone as the photoinitiator, BAPO is a stronger choice for this product specifically. The Kerai et al. (2015) study did not use a filler that would disperse light as silver phosphate glass does. They also chose 2-hydroxy-2-methylpropiophenone specifically for its non-yellowing properties, but the aesthetics of this design are inconsequential, as it is concealed (19). Since BAPO has a deep curing profile from its photobleaching properties, it is more effective against the curing conflict that silver phosphate glass creates than 2-hydroxy-2-methylpropiophenone (25). Furthermore, BAPO has an absorption window of λ = 360–440 nm, which is closer to the range of common salon lamps, like SUNUV, which is a dual-wavelength 365/405 nm LED lamp (36). Furthermore, as a result of the EU banning TPO, a

widely used photoinitiator, BAPO has become one of the most popular alternatives in UV-cured nail supplies (39).

MEHQ is a standard additive for shelf stability, and the silver phosphate glass will be treated with MPS in order to prevent sticking.

Proposed Experiment Design

Stage 0: Calculating Silver Release Rate

The silver release from the silver phosphate glass in order to effectively kill *P. aeruginosa* without being cytotoxic can be estimated. For this calculation, I used the concentration range, 0.1 ppm to 1.6 ppm, found by P. Saravanapavan et al. It should be noted that it is unclear whether those concentrations are per day, hour, week, etc (32).

I first estimated the area of the nail bed as 130 mm^2; then, assuming roughly a third of that area would lift, though that fraction varies, I found the total area of the lifted pocket to be 45 mm^2. Estimating the height of the pocket as 0.05 mm, I found the volume of the pocket to be 0.00225 mL. I multiplied that volume by the minimum and maximum concentrations separately to find that the range of the amount of silver that can be in the pocket per day is 0.000225 µg to 0.0036 µg. The target silver release rate was found by dividing the amount of silver by the area of the lifted pocket. I estimated the target release rate range to be 0.000005 µg/mm^2 to 0.00008 µg/mm^2 per day.

Finding the target silver release rate revealed that the amount of filler in the gel at any wt% will be higher than the required amount of filler for 28 days. Therefore, the amount of filler is not a constraint; rather, the silver release rate is. I used Valappil's 1.27 µg/mm^2 per hour dissolution rate for the Ag3 glass with ~6% of the mass being silver to calculate .078 µg/mm^2 silver released per hour, which is about 23,000x faster than the maximum release rate. Hence, experimentation is looking for the best way to slow down the silver release rate to stay within the 0.000005 µg/mm^2 to 0.00008 µg/mm^2 per day rate range.

Stage 1: Silver Phosphate Glass Composition

The optimal silver phosphate composition will be found through testing three different compositions for degradation rates shown in Figure 4. The results from the Valappil et al. study on silver phosphate glass can be used to conduct a screening of the silver phosphate glass. Valappil et al. specifically studied silver phosphate glass against *P. aeruginosa*, and they found 50 P_2O_5 – 30 CaO – 17 Na_2O – 3 Ag_2SO_4 was within the cyto-/biocompatibility range (42). It was decided to use that composition as a baseline to test for the best dissolution rate for 2-4

weeks of use. It was also shown that higher CaO concentration results in slower degradation rates; however, slower dissolution means less antimicrobial activity (40). Each composition with different concentrations of CaO will be tested for degradation rate, silver release rate, photostability in the dark and when exposed to UV light, amorphousness, pH, and glass discoloration.

Six tests will be run, as each composition will be tested in darkness and in UV exposure to test for photostability. The compositions in the UV arm will be exposed to dual-wavelength 365/405 nm LED light to imitate the real application. The compositions in the dark will act as a control to measure the UV-exposed compositions against; this way, we can find whether the UV caused discoloration, degradation rate, or changes in Ag charge. Before and after the experiments are run, XRD and XANES will be used to test for amorphousness and to confirm that the silver ions keep a +1 charge. A discoloration test using colour measurement will also be added before and after the tests are run.

The glass will be ground into a powder and measured for surface area using the BET method. It will be submerged in 37 °C deionized water, replacing the solvent at time intervals (6, 24, 48, 120, and 168 h; and weekly until 28 days) to prevent saturation, similar to Valappil et al. methods (42). At each time point, total silver will be measured by ICP-MS, and Na^{+}, Ca^{2+}, and phosphate dissolution will be measured with ion chromatography and used with surface area to find the degradation rate and ensure the glass dissolves steadily. Additionally, pH will be measured at every time point.

The chosen glass composition will have the slowest silver release rate, staying above the minimum from Stage 0.

Table 2.

	P_2O_5	**CaO**	**Na_2O**	**Ag_2SO_4**
Faster Rate	50 mol%	25 mol%	22 mol%	3 mol%
Valappil's Rate	50 mol%	30 mol%	17 mol%	3 mol%
Slower Rate	50 mol%	35 mol%	12 mol%	3 mol%

The table displays release rates of three glass compositions with expected release rates relative to previous material.

It is important to note that the resulting silver release rates will be significantly faster than when it is formulated into the gel. Furthermore, the silver phosphate glass will not be in deionized water in reality; instead, the moisture under the nail enhancement will be a mix of salt, sweat, oil, and other external substances.

Stage 2: Gel Formulation

Once a composite is chosen, stage 2 will determine the amount of filler needed to keep the formula optically clear, test the cure length, and verify that the silver ions remain positively charged.

Five formulations of UDMA, EMA, BAPO, and MEHQ with different concentrations of glass treated with MPS will be made. As found in Stage 0, the silver release rate needs to be significantly lowered. Hence, low weights were chosen for testing as they will have the best chance to decrease the release rate.

Table 3.

	Silver Phosphate Glass (wt%)
F1	0%
F2	0.5%
F3	1%
F4	2%
F5	3%

Each formula will be mixed, then brushed onto 3 different slides with a typical gel nail polish brush. The thickness should then be measured by a micrometer to ensure it is close to 0.03 mm. They will then be cured for 60 seconds under a dual-wavelength 365/405 nm salon LED lamp, and the tacky oxygen inhibition layer will be wiped with isopropanol. All slides will be tested for clarity using a spectrometer to measure how much light passes through the gel as the filler scatters it, degree of conversion using FTIR to measure the amount of hardened gel, and discoloration of the silver ions against control using XANES (F1). It is also important to report the rheology of the gel, so notes will be taken on viscosity and brushability of the gel.

A color difference against F1 below the threshold for visibility to the human eye, subsequent brushability, and a degree of conversion close to that of F1 are the requirements for a functional formula. The formula with the lowest concentration of silver phosphate glass will be chosen as long as it meets those requirements.

Stage 3: Ion Release After Formulation

Once the silver phosphate glass composition and its concentration within the gel are chosen, the actual silver release rate can be measured. The ion release rate that was measured in stage one was with the glass on its own in order to ensure there was a linear rate without an initial burst. In stage three, the release rate will be tested to see if 28 days of ion release is feasible when the chosen glass composition is mixed into the gel formula at the chosen filler weight percentage.

The loading selected in Stage 2 will be tested as well as one additional loading that met the Stage 2 requirements. Each loading formula will be brushed onto 3 different slides with a typical gel nail polish brush. The thickness should then be measured by a micrometer to ensure it is close to 0.03 mm. They will then be cured for 60 seconds under a dual-wavelength 365/405 nm salon LED lamp, and the oxygen inhibition layer will be wiped with isopropanol. They will then be flipped and placed over a well of 0.045 mL of deionized water, which is the volume of the pocket scaled up by 20. Note that the area of the gel was also scaled by 20. Then, silver release will be measured using ICP-MS at days 1, 3, 7, 14, 21, and 28, replacing the water at each time point. The release rates will be plotted for each interval in order to confirm they are within the release rate range from Stage 0 and that there is steady release. Additionally, there should still be silver remaining at the end of the 28 days.

It is plausible this stage will fail, meaning the release rates were too fast, too slow, or non-linear. Most likely, the rate would be too fast, as the optimized resin, composition, and filler weight did not slow it down enough. In that case, the formula may need to be more water-resistant, have a lower filler concentration, or the glass composition needs to be slower. In the case that the release is too slow, filler loading should be raised, composition should be faster, and the formula should be less water-resistant. Furthermore, if there is an initial burst, it may be caused by loose particles that are not suspended in the gel. Therefore, an additional coat of plain gel may be added on top of the antimicrobial interface to seal loose particles.

It is important to note that a slide with a film on it over deionized water does not properly mimic a lifted pocket of water between a keratin nail and the silver-containing layer.

Stage 4: Antimicrobial Effectiveness

Testing for whether the formulation from the last stages is effective against *P. aeruginosa* will be conducted in 3 separate arms: Gel with silver phosphate glass, gel without silver phosphate glass, and a control with a known killer of *P. aeruginosa*. I will also include a sterility control with nothing on it to ensure there was no contamination.

The process of evaluating the antimicrobial activity will follow the ISO 22196 standard. The bacteria will be grown overnight and diluted to a standard concentration. Then a very small

volume of that solution will be pipetted onto a disc with a .03 mm thick layer of silver-containing gel, normal gel, the known killer of *P. aeruginosa,* or nothing. It will be covered and incubated for a standard 24 hours. After 24 hours, the remaining bacteria will be rinsed off into a silver-neutralizing solution. Then, to make the bacteria countable, the solution can be diluted until the number of bacteria is in a suitable range. Once counted, the actual number of bacteria that survived can be calculated and compared to the control, the gel without silver phosphate glass. This experiment will be repeated at days 1, 7, 14, 21, and 28 using 5 different aged sets of 4 discs.

The criterion for percent organisms killed is the standard 99.9% bar. If the test fails because of early burst, return to stage 3. If the percent killed is less than 99.9%, the 0.1 ppm minimum may not have been a valid estimate for this design. Therefore, it would be necessary to go back to the original range and find a more accurate one.

The limitations of this stage include the moderately unrealistic setup of the experiment as well as the *P. aeruginosa* strains possibly not acting the same as clinical isolates.

Stage 5: Mechanical Testing

Strong adhesion and resistance to mechanical pressure are both critical elements of this design. The silver-infused gel should be able to bond to a keratin nail plate just as well as a normal gel adhesive. I decided to follow the modified cross-cut adhesion testing from ISO 2409:2013 used by Kerai et al. in their study of using UV-curable gel as a drug carrier (19). However, it is worth nothing Kerai et al. used a high-density polyethylene, but a keratin substrate is proposed for this design because it is more clinically relevant. Additionally, the substrate will be buffed, and a nail primer will be applied to imitate a normal salon routine. Furthermore, all tests will be done at the beginning and end of a 28-day cycle. The cycle would include wet and dry environments every day for the entire time period in order to imitate hand-washing, showers, etc.

The gel will be cured in a .03 mm layer onto a buffed and primed keratin substrate, like bovine hoof, and left for 24 hours. The adhesion will then be measured by cutting a cross-hatch pattern using a scalpel. Six parallel cuts to the gel application direction will be made, and then six additional perpendicular cuts. Loose film will be removed with a soft brush backwards, forwards, and diagonally. It can then be visually assessed for which pieces of gel were removed from the substrate. The test will be scored on the same scale as the previous study: 0 = layer is totally unaffected; 1 = under 5% of lattice film area is affected with some small flakes of film slightly lifting; 2 = in between 5% and 15% of film area is affected and it has flaked on the edges or intersections of the cuts; 3 = there is partial or whole flaking along the edges in large ribbons with $\geq$15% but $\leq$35% being affected; 4 = there is complete detachment of the squares to the substrate or full lifting along the edges in large ribbons with >35% but <65% being affected; 5 = any degree of detachment not categorized from 0-4. Higher scores indicate poor adhesion and

less resistance of the film's removal from the substrate (19). This test will be repeated for the gel without silver phosphate glass as well as a commercial gel adhesive.

The interlayer must also bond well to a commercial UV-curable gel adhesive, as the silver layer will sit in between the nail plate and the commercial adhesive. Hence, the ISO 4624 pull-off test will be utilized to test the bond between the silver layer and the commercial gel (14). My interlayer will be applied at .03 mm of thickness to a keratin substrate, then the commercial gel will be applied on top. It should be noted that for this test, the oxygen inhibition layer should not be wiped, as it would not be in salon practice. The general method for testing will then be carried out. The results of the test should show the commercial gel is sufficiently bonded to the interface layer when compared to the commercial gel's bond with the substrate.

Furthermore, this stage will also test for flexibility, as it is important that the gel molds with the curve of the natural nail. A three-point bending test following the ASTM D790 standard test method will be used to determine flexibility (3). The flexibility numbers should match those of the unfilled gel. In a previous study using silver phosphate glass in a methacrylate polymer, the flexibility and microhardness were found to be the same. Yang and Lee used silver phosphate glass concentrations of 0-8 wt%, which are larger than my concentrations (43). Therefore, this suggests that the flexibility test is likely to pass.

These tests do not match an actual wear test over 28 days of handwashing, showering, and other daily activities. Furthermore, a keratin substrate is not the same as a real nail plate with sweat, oils, and other external substances. Mechanical stress in a real application of this design also differs from the mechanical stress applied with the flexibility test.

Stage 6: Biocompatibility

Since this project is meant for people with a weakened immune system, it is critical that the gel is safe in terms of cytotoxicity, allergy risk, and silver staining. The gel was formulated using the 1.6 ppm cytotoxicity bar, so it is expected that the silver is not harmful. Additionally, the most common allergy-causing ingredient, HEMA, was replaced in the formula. Furthermore, a widely used photoinitiator, TPO, was also replaced as it is a reproductive toxicant.

Whether the gel is cell-killing or not can be tested using the standard ISO 10993-12 method (15). An extract will be obtained by placing cured film into cell culture liquid. That extract will be placed on a dish with living skin cells and connective tissue cells, the cells that live around the nail. The number of living cells will be counted using an MTT assay, as used in Yang and Lee's biocompatibility testing (43). This method will be used on the silver-infused gel, a non-silver control gel, and a higher concentration gel. The higher concentration gel is added because the real pocket was 45 mm^2 per .00225 mL, or 200 cm^2 per mL, while the ISO 10993-12 standard is usually 3 cm^2 per mL. Hence, the actual pocket has a much higher concentration, so that should

be taken into consideration as it may affect cytotoxicity. If 70% or more of the cells survive compared to the control, the test passes based on the standard. If the test fails, stage 3 should be revisited.

Although TPO and HEMA were removed from the formula, all methacrylates carry the risk of allergy (10). The risk is most prevalent when the gel is uncured, so it is essential that the degree of conversion found in Stage 2 is high enough for a complete cure. If there is a significant amount of unreacted monomers after curing, there is a high risk of contact dermatitis allergy. Hence, following the tests for unreacted monomers used by Kerai et al., ultrasonic extraction will be utilized. Kerai et al. found an extremely low amount of unreacted monomers, so it can be expected that my results will be alike, as we used similar monomers. If this fails, the formulation may need to be adjusted or the cure time lengthened.

Since silver bonds to keratin, dark gray or black staining of the nail plate may occur over time (37). It would be preferable if this were avoided for cosmetic reasons. A 28-day, wet and dry cycled test of the interlayer and a non-silver gel on a keratin substrate will be run to determine the color difference between the experiment and the control. That difference should be under the threshold of visibility to the human eye. If there is silver staining, it may need to be considered whether it is outweighed by the benefits of using silver.

Formal patch testing on people is not feasible for the scope of this project, but it would be required for commercialization. Also, the skin cells and connective tissue cells in a dish do not replicate an immunocompromised person's nail plate.

Future Research

The scope of this paper only covers a portion of the research required to turn this design into a usable product. In following through with my proposed tests and methods, there will likely be specifics that I did not cover. Hence, in reality, the use of other or additional methods is probable, and additional research could be conducted if these tests are run.

Conclusions

Ideally, this would give recovering chemotherapy patients an additional option for salon services while their immune system is still compromised. If this research were fully completed with actual testing, it would be determined whether making an antimicrobial, UV-curable gel using silver phosphate glass is attainable or not.

Although this product specifically targets those who have gone through chemotherapy and immunocompromised individuals in general, the audience that this affects is much greater. People who regularly get their nails done are at risk of infection, even though it is not particularly dangerous or pressing for healthy individuals; however, if those people ever come

into contact with someone immunocompromised, which the CDC lists as a way the disease spreads, that poses a severe risk (1).

Additionally, this product remains a contribution to the nail industry by possibly becoming a standard in nail salons, or more realistically, a catalyst for more products targeting *P. aeruginosa* infections in nails being manufactured and researched.

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