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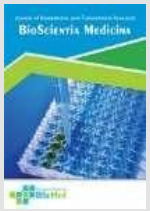

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VAT Dyes as Primary Sensitizers in Occupational Contact Dermatitis: Clinical and Patch Test Profiles in the Traditional Sasirangan Textile Industry

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A B S T R A C T

Background: Occupational contact dermatitis (OCD) significantly impacts workers in the informal textile sector. While disperse dyes are well-documented sensitizers, the allergenic potential of VAT dyes in traditional manufacturing, such as the Indonesian Sasirangan batik industry, remains under-evaluated. **Methods:** An analytical observational cross-sectional study was conducted on 40 Sasirangan artisans (20 wet workers, 20 dry workers). Clinical diagnoses were established using the Mathias criteria and NOSQ-2002. Epicutaneous patch testing was performed using a baseline series and specific synthetic dyes (1% in petrolatum), read at 48, 72, and 96 hours per ICDRG criteria. Multivariable logistic regression complemented the primary statistical analysis to assess predictive risk factors. **Results:** The prevalence of positive patch tests was 62.5% (25/40). The primary sensitizers were VAT dye willanthrene brill rose 4R (42.5%) and VAT dye willanthrene green B (37.5%). A significant correlation was found between a clinical history of OCD and positive patch test outcomes (p=0.014, OR=5.6). Surprisingly, job type (wet vs. dry), handwashing frequency, and PPE use did not significantly correlate with patch test positivity (p>0.05), highlighting the pervasive nature of dye allergens across the workspace. **Conclusion:** VAT dyes are potent primary sensitizers in the traditional Sasirangan textile industry. A clinical history of OCD is a strong predictor of patch test positivity, emphasizing the need for targeted allergen identification and barrier protection.

1. Introduction

Occupational skin diseases represent a pervasive, escalating, and profoundly debilitating global health challenge, consistently ranking among the most frequently diagnosed work-related illnesses across both highly industrialized nations and rapidly developing economies. Within this broad and diverse category of occupational pathologies, occupational contact dermatitis accounts for an overwhelming and disproportionate majority, comprising more than ninety percent of all documented work-related cutaneous cases. The ramifications of occupational contact dermatitis extend far beyond superficial cutaneous symptoms; it constitutes a massive socioeconomic burden on a global scale. The disease trajectory is frequently chronic, recalcitrant, and prone to severe exacerbations, leading to substantial economic consequences driven by prolonged and specialized medical treatments, frequent absenteeism, and a significant, quantifiable reduction in overall workplace productivity.[1] Furthermore, the persistent nature of severe occupational contact dermatitis frequently forces highly skilled and experienced workers into premature occupational retraining or complete, permanent withdrawal from the active workforce. This dynamic drastically compounds the financial strain on affected individuals, their dependent families, and public healthcare systems

alike. The psychosocial impact, which includes a severely diminished quality of life, debilitating chronic pruritus, severe sleep disturbances, and intense social stigmatization due to visible, aesthetically displeasing skin lesions, further underscores the absolute severity of this persistent occupational hazard.

The profound burden of occupational contact dermatitis is disproportionately amplified within the informal industrial sectors of developing nations.[2] Unlike formal corporate manufacturing environments, which are typically governed by highly regulated, stringently enforced occupational safety and health standards, the informal sector is characterized by decentralized, highly unregulated, small-scale, and frequently home-based manufacturing units. This informal sector absorbs a massive, continuously growing segment of the vulnerable workforce, particularly in developing regions across Southeast Asia, providing crucial, irreplaceable livelihood opportunities for millions of marginalized individuals. However, this essential economic lifeline is inherently fraught with severe, unmitigated vulnerabilities. Workers operating within the informal sector frequently perform their duties in poorly ventilated, structurally inadequate environments entirely devoid of mechanized safety infrastructure, standardized chemical hazard communication protocols, or routine occupational medical surveillance. Consequently, they are routinely and heavily exposed to a myriad of physical, chemical, and biological hazards without the fundamental mitigation provided by standardized engineering controls or administrative oversight. The complete absence of systematic occupational safety and health enforcement leaves these highly vulnerable populations entirely dependent on inadequate, improvised, or self-procured personal protective equipment, which frequently fails to provide a sufficient or reliable physical barrier against highly aggressive, corrosive industrial chemicals.

Among the various specialized informal manufacturing domains, the textile and garment production industries are internationally recognized as exceptionally high-risk environments for the pathogenesis and rapid development of both irritant contact dermatitis and allergic contact dermatitis. The etiology of occupational contact dermatitis among textile artisans is highly complex, synergistic, and inherently multifactorial.[3] The manual production of textiles requires continuous, prolonged human physical interaction with an extensive array of harsh synthetic chemical compounds, aggressive mechanical friction processes, and unfavorable, high-humidity microclimatic conditions. The primary, foundational driver of dermatitis pathogenesis in these specific settings is the relentless, daily degradation of the protective epidermal barrier. Workers are subjected to continuous wet work, clinically defined as the total immersion of hands in aqueous liquids for extended periods exceeding two hours per shift, or the exceptionally frequent washing and rinsing of hands. Prolonged exposure to these aqueous environments induces profound hyperhydration of the stratum corneum, rapid swelling of individual corneocytes, and the subsequent structural disruption of the critical intercellular lipid lamellae. This microscopic structural compromise drastically increases transepidermal water loss and significantly lowers the natural threshold for percutaneous chemical penetration.

Furthermore, the foundational textile dyeing process heavily relies on the extensive utilization of robust alkaline agents, including high concentrations of sodium hydroxide and sodium hypochlorite, which serve essential chemical roles as mordants, reducers, and bleaching agents. These highly potent alkaline chemicals act as aggressive primary irritants by directly saponifying vital epidermal surface lipids, denaturing structural keratins within the epidermis, and drastically shifting the natural acidic pH of the skin mantle to a pathological alkaline state. The synergistic, compounding effect of chronic wet work, severe mechanical friction resulting from handling coarse, heavily bound fabrics, and the corrosive, burning nature of these alkaline solutions completely dismantles the natural defensive barrier of the skin. This complete barrier failure creates an optimal,

highly permeable pathway for the percutaneous absorption of low-molecular-weight sensitizing haptens directly into the viable epidermis, where the immunological cascade of dermatitis is initiated.[4]

Within the vast spectrum of chemical hazards present in the textile manufacturing industry, synthetic dyes represent the most significant and thoroughly documented immunologic threat. Historically, dermatotoxicological research and clinical investigations have predominantly focused on disperse dyes as the most notorious and aggressive sensitizers responsible for textile-related allergic contact dermatitis. Disperse dyes are characterized by their specific physiochemical properties, namely their extremely low molecular weight, pronounced lipophilic nature, and relatively weak physical affinity for synthetic and natural fibers.[5] These specific properties allow disperse dye molecules to readily detach from finished textiles, dissolve rapidly into human sebum or sweat, and easily penetrate the intact stratum corneum to initiate a potent, cell-mediated Type IV delayed hypersensitivity reaction. Consequently, disperse dyes have been extensively documented, thoroughly researched, and universally included in standardized diagnostic patch test baselines across global dermatology clinics.

Conversely, synthetic VAT dyes have traditionally been perceived by the occupational dermatology community as posing a significantly lower risk for inducing allergic sensitization. From a purely chemical perspective, VAT dyes are highly complex, large-molecular-weight compounds that are inherently water-insoluble in their stable, natural state.[6] Because they cannot directly impregnate or bind to cellulose fibers while insoluble, the industrial application of VAT dyes requires a highly specific, intricate, multi-step reduction and oxidation chemical process. The totally insoluble dye must first be aggressively reduced in a strongly alkaline chemical bath—typically utilizing boiling sodium hydroxide and sodium dithionite—to convert the molecule into a temporary, water-soluble, highly substantive leuco form. It is exclusively in this chemically reduced state that the dye can physically penetrate the microscopic matrix of the textile fiber. Subsequent exposure to ambient oxygen or liquid oxidizing agents forces the leuco form to revert completely back into its original, insoluble, brightly colored state, permanently trapping the massive pigment molecules securely within the intricate matrix of the cellulose fiber. Because the final, oxidized dye is completely water-insoluble and firmly locked mechanically into the textile, it theoretically resists any leaching onto human skin through sweat or friction. This theoretical stability has led to the widespread clinical assumption that VAT dyes are highly unlikely to elicit severe allergic contact dermatitis in end-consumers or workers.

However, this theoretical toxicological assumption fundamentally fails to account for the harsh occupational realities and intense chemical exposures experienced by the artisans who are directly mixing, applying, and handling these chemicals in their raw, unreacted, or chemically active reduced states during the actual manufacturing process.[7] This specific, severe hazard profile is vividly and tragically illustrated in the contemporary production of Sasirangan, a deeply revered, traditional heritage textile native to South Kalimantan, Indonesia. Historically, the vibrant, culturally significant colors of Sasirangan cloth were achieved exclusively through the meticulous application of natural plant and root extracts, which posed absolutely minimal toxicological or immunological risks to the artisans. However, in order to successfully meet the rapidly escalating commercial demands of modern mass production, reduce overall manufacturing costs, and achieve broader, significantly more resilient color palettes, the contemporary Sasirangan industry has undergone a complete, unregulated chemical shift. The daily manufacturing process now relies completely upon the heavy utilization of potent synthetic chemicals, primarily complex synthetic VAT dyes, naphthol coupling compounds, and massive, poorly regulated quantities of robust alkaline reducing agents like sodium hydroxide.

The physical creation of Sasirangan involves highly intricate, physically demanding manual labor that forces these traditional artisans into direct, continuous, and unprotected physical contact with these hazardous chemical substances. The complex production cycle is strictly divided into distinct operational phases, with each phase carrying unique, severe occupational dermatological exposures.[8] The initial tying phase involves meticulously binding the raw fabric with extremely tight, coarse threads to create the necessary resist patterns, an action that exerts immense, repetitive mechanical friction on the digits and palms, leading to profound hyperkeratosis, painful fissuring, and continuous microtrauma of the epidermal barrier. This is immediately followed by the dipping phase, a severe wet work hazard where artisans manually submerge the tightly tied fabrics directly into deep vats containing the highly alkaline, chemically reduced leuco-VAT dye solutions, almost entirely by hand. Finally, the untying phase represents a severe dry work hazard, where artisans meticulously slice and remove the binding threads from the completely dried, heavily dyed fabric. This intense dry process generates significant friction and releases microscopic, un-fixed VAT dye dust particles directly into the immediate breathing zone and onto the compromised, sweating skin surfaces of the workers.

Throughout these highly laborious, repetitive stages, the utilization of standardized, high-quality, chemically resistant personal protective equipment is virtually nonexistent.[9] Deep-rooted cultural working habits, severe financial constraints within the informal economy, and a total lack of structured occupational health literacy result in artisans routinely performing these highly toxic tasks entirely barehanded or while utilizing completely inadequate, highly permeable fabric barriers that paradoxically trap the corrosive, sensitizing liquids directly against the skin, thereby drastically exacerbating the chemical insult. Consequently, an alarmingly high prevalence of severe, visible skin morbidities—ranging from profound xerosis and deeply painful palmar fissuring to widespread, acutely vesicular, weeping eczematous lesions—is consistently and frequently reported among these dedicated traditional workers.

Despite the undeniable, overwhelming clinical evidence of profound, widespread occupational skin disease within this specific artisan population, empirical scientific data pinpointing the exact immunological triggers and causative haptens remain critically and alarmingly scarce. The highly complex immunological interplay between the severe alkaline-induced destruction of the epidermal barrier and the potent sensitizing potential of raw, reduced VAT dye monomers in a chaotic occupational setting has not been adequately or systematically investigated. The prevailing scientific literature completely lacks detailed, statistically robust epidemiological studies utilizing highly specific, chemically calibrated epicutaneous patch testing to identify the exact hapten-carrier protein complexes driving the severe delayed-type hypersensitivity observed in these specific artisans. This vast, unaddressed knowledge gap severely hinders the crucial development of targeted diagnostic testing protocols, evidence-based dermatological medical interventions, and effective, culturally appropriate preventative workplace safety strategies. There is an immediate, urgent scientific need to systematically and thoroughly dissect the detailed dermatotoxicological profile of this informal traditional industry to effectively mitigate the rapidly escalating occupational health crisis currently devastating its vulnerable workforce.[10] The primary aim of this study is to profile the specific sensitizing allergens causing occupational contact dermatitis and to analyze the correlation between clinical history and epicutaneous patch test outcomes among Sasirangan artisans. The novelty of this research lies in its unprecedented focus on synthetic VAT dyes as primary sensitizers in a traditional, informal textile setting, providing a deep exploration into the pathophysiology of VAT dye-induced delayed-type hypersensitivity—a domain that remains largely unmapped in contemporary dermatotoxicology.

2. Methods

Study design and population

An analytical observational study with a cross-sectional design was executed in the Kampung Sasirangan industrial center, Banjarmasin, Indonesia. Purposive sampling was utilized to recruit 40 active Sasirangan textile artisans who met the inclusion criteria: continuous employment for at least one month, minimal to no standardized PPE usage during chemical handling, and willingness to undergo 96-hour epicutaneous patch testing. Exclusion criteria included the use of systemic corticosteroids within 6 weeks or topical corticosteroids/UVB therapy within 4 weeks prior to the study, and the presence of acute, widespread dermatitis. Subjects were stratified into two distinct exposure groups: Wet Workers (n=20, primarily involved in dye mixing and fabric dipping) and Dry Workers (n=20, involved in pattern sewing, thread cutting, and ironing).

Clinical evaluation and questionnaires

Baseline demographic and occupational data, including age, gender, education, work duration, dipping duration, handwashing frequency, and PPE usage, were recorded. The clinical diagnosis and history of OCD were systematically evaluated utilizing the Nordic Occupational Skin Questionnaire (NOSQ-2002/LONG) and the standardized Mathias Criteria for occupational causality. A Mathias score of ≥ 4 out of 7 criteria established a positive history of OCD.

Patch testing procedure

Epicutaneous patch testing remains the gold standard for identifying the causative hapten in ACD. The testing utilized standard IQ Ultra chambers applied to the upper back, avoiding the scapular and midline regions to prevent detachment. The allergen panel included standardized baseline allergens (Patch Gen) alongside targeted, own material occupational allergens prevalent in the Sasirangan industry. The custom textile dye allergens were synthesized at a 1% concentration in a petrolatum (pet) vehicle, a concentration specifically calibrated to elicit an immunological response without triggering primary irritant dermatitis. The targeted allergen panel included: (1) VAT dye willanthrene brill rose 4R 200 (1% pet); (2) VAT dye willanthrene brown BR 200 (1% pet); (3) VAT dye willanthrene green B (1% pet); (4) VAT dye willanthrene violet RR 100 (1% pet); (5) VAT dye willanthrene blue RSN 200 (1% pet); (6) VAT dye willanthrene yellow GCN 100 (1% pet); (7) Naphthol ASBO (1% pet); (8) Sodium hypochlorite (1% aq); (9) Sodium hydroxide (1% aq); (10) Para-phenylenediamine (PPD) (1% pet). Patches were removed after 48 hours. Readings were conducted at 48, 72, and 96 hours post-application. Morphological reactions were graded strictly according to the International Contact Dermatitis Research Group (ICDRG) criteria: negative (-), doubtful (?+), weak positive (+), strong positive (++), extreme positive (+++), or irritant reaction (IR).

Statistical analysis

Data were analyzed using SPSS version 25.0. Descriptive statistics summarized demographic and occupational variables. Normality was assessed via the Shapiro-Wilk test. Categorical variables were evaluated using Pearson's Chi-square or Fisher's Exact tests, where expected cell counts were <5. The strength of association was evaluated via Spearman's rank correlation. To enhance methodological rigor, a multivariable logistic regression model was constructed to identify independent predictors of positive patch test outcomes, adjusting for age, gender, and job type. A p-value of <0.05 was considered statistically significant.

3. Results

The demographic and occupational characteristics of the study cohort (N=40) are detailed in Table 1, stratified by exposure type into wet (n=20) and dry (n=20) textile workers. The median age of the total cohort was 30 years (range: 19–55), with no statistically significant age variance between the two occupational subsets (p=0.450). Males constituted 60% of the overall population; however, a highly

significant gender disparity was observed between job roles (p=0.001). Specifically, the wet worker cohort, responsible for physically demanding chemical dipping, was predominantly male (90%), whereas the dry worker cohort, tasked with precise sewing and untying, was primarily female (70%). Occupational exposure chronicity was comparable across groups, with a median overall employment duration of 4.8 years (p=0.218). Analysis of the wet workers' specific behavioral patterns revealed intense chemical exposure, as 45% engaged in fabric dipping for over five hours daily, and 60% washed their hands more than five times per shift. Alarmingly, adherence to comprehensive occupational safety protocols was uniformly poor. While all participants reported the sporadic use of protective gloves, the utilization of high-tier barrier protection was negligible; none utilized protective aprons, and only 20% of the high-risk wet workers utilized eye goggles.

Table 1. Demographic and Occupational Characteristics of Sasirangan Artisans

Variables	Total Cohort (N = 40)	Wet Workers (n = 20)	Dry Workers (n = 20)	p-value
Demographic Characteristics				
Age (years), median (range)	30 (19 – 55)	31 (21 – 54)	29 (19 – 55)	0.450
Gender, n (%)				
Male	24 (60.0%)	18 (90.0%)	6 (30.0%)	0.001*
Female	16 (40.0%)	2 (10.0%)	14 (70.0%)	
Occupational Characteristics				
Employment Duration (years), median	4.8	4.5	5.0	0.218
Daily Dipping Duration, n (%)				
> 5 hours/day	-	9 (45.0%)	N/A	-
≤ 5 hours/day	-	11 (55.0%)	N/A	-
Handwashing Frequency, n (%)				
> 5 times/shift	-	12 (60.0%)	N/A	-
≤ 5 times/shift	-	8 (40.0%)	N/A	-
Personal Protective Equipment (PPE) Usage				
Sporadic Glove Use	40 (100%)	20 (100%)	20 (100%)	1.000
Protective Apron	0 (0%)	0 (0%)	0 (0%)	-
Eye Goggles	4 (10.0%)	4 (20.0%)	0 (0%)	0.106

Note: * Statistically significant ($p < 0.05$). N/A indicates the characteristic is not applicable to the designated occupational role (dry workers do not engage in VAT dye dipping).

Table 2 delineates the precise epicutaneous patch test outcomes stratified by occupational exposure, highlighting synthetic VAT dyes and alkaline reducing agents as the primary culprits of contact sensitization among Sasirangan artisans. The data reveal a profound immunological response to VAT dyes, with willanthrene brill rose 4R emerging as the most prevalent sensitizer, eliciting positive reactions in 42.5

percent of the total cohort. This was closely followed by willanthrene green B, which sensitized 37.5 percent of the participants. Interestingly, dry workers exhibited a markedly higher sensitization rate to willanthrene green B (50.0 percent) compared to wet workers (25.0 percent), underscoring the severe risk posed by airborne dye dust and contaminated dry fabrics during the untying process. Furthermore, alkaline chemicals utilized in the reduction phase demonstrated substantial dermatotoxicological impact. Sodium hydroxide induced severe reactions—clinically challenging to differentiate between extreme irritant and weak allergic responses—in 37.5 percent of the cohort, predominantly affecting wet workers (50.0 percent). Other synthetic additives, including naphthol ASBO and para-phenylenediamine, played a secondary role, each sensitizing only 5.0 percent of the population. These findings unequivocally confirm that complex VAT dyes act as aggressive occupational allergens, facilitated by severe alkaline-induced epidermal barrier disruption. Polysensitization (reactions to >1 allergen) was observed in 68% (n=17) of the positively tested subjects. Reaction intensity was notable, with 25% of positive subjects displaying strong (++) reactions characterized by intense erythema, induration, and vesiculation by the 96-hour reading.

Table 2. Profile of Epicutaneous Patch Test Results by Occupational Group

Tested Allergen (1% Concentration)	Wet Workers (n = 20)	Dry Workers (n = 20)	Total Positive (N = 40)
Synthetic VAT Dyes (Primary Sensitizers)			
VAT dye willanthrene brill rose 4R	8 (40.0%)	9 (45.0%)	**17 (42.5%)**
VAT dye willanthrene green B	5 (25.0%)	10 (50.0%)	**15 (37.5%)**
VAT dye willanthrene violet RR 100	3 (15.0%)	0 (0.0%)	3 (7.5%)
Alkaline Reducing & Bleaching Agents			
Sodium hydroxide (IR/+)	10 (50.0%)	5 (25.0%)	**15 (37.5%)**
Sodium hypochlorite (IR/+)	3 (15.0%)	4 (20.0%)	7 (17.5%)
Other Synthetic Additives			
Naphthol ASBO	2 (10.0%)	0 (0.0%)	2 (5.0%)
Para-phenylenediamine (PPD)	2 (10.0%)	0 (0.0%)	2 (5.0%)

Notes: Values are presented as number of subjects (percentage of group total). Reactions graded as weak positive (+), strong positive (++), or extreme positive (+++) according to ICDRG criteria are recorded as positive. **IR/+** indicates cases where clinical differentiation between severe Irritant Reaction (IR) and weak allergic positive (+) was morphologically challenging at 96 hours.

Figure 1 presents a comprehensive evaluation of the predictive variables associated with epicutaneous patch test positivity among the traditional textile artisan cohort, utilizing both bivariate correlation and multivariable logistic regression modeling. Panel A illustrates the profound diagnostic utility of establishing a standardized clinical history prior to chemical testing. Strikingly, every subject possessing

a definitive clinical history of occupational contact dermatitis, determined by a Mathias Criteria score of four or greater, exhibited a positive patch test outcome. This absolute concordance yields a highly significant statistical correlation (p=0.014, Spearman rank correlation coefficient 0.387), confirming that structured clinical anamnesis serves as a robust prognostic indicator for true allergic sensitization in this specific occupational setting.

Panel B visualizes the results of the multivariable logistic regression model through a detailed forest plot, assessing the independent predictive value of various clinical and occupational risk factors while controlling for confounding variables. The vertical reference line denotes an adjusted odds ratio of 1.0, indicating a null effect. The analysis unequivocally isolates a clinical history of occupational contact dermatitis as the sole statistically significant independent predictor of patch test positivity, increasing the likelihood of a positive reaction by a factor of 5.6 (95 percent confidence interval: 1.2 to 25.8; p=0.021).

Conversely, specific task-related occupational variables entirely failed to achieve statistical significance. Job classification distinguishing wet versus dry work, daily dipping durations exceeding five hours, and high-frequency handwashing yielded adjusted odds ratios closely approximating the null value, with wide confidence intervals crossing the reference line. These statistical findings strongly suggest that the fundamental dermatotoxicological hazard is not exclusively isolated to specific high-intensity wet tasks. Instead, the potent sensitizing agents are pervasively distributed throughout the entire manufacturing microenvironment, emphasizing the paramount importance of thorough clinical history over isolated occupational task variables in predicting allergic sensitization.

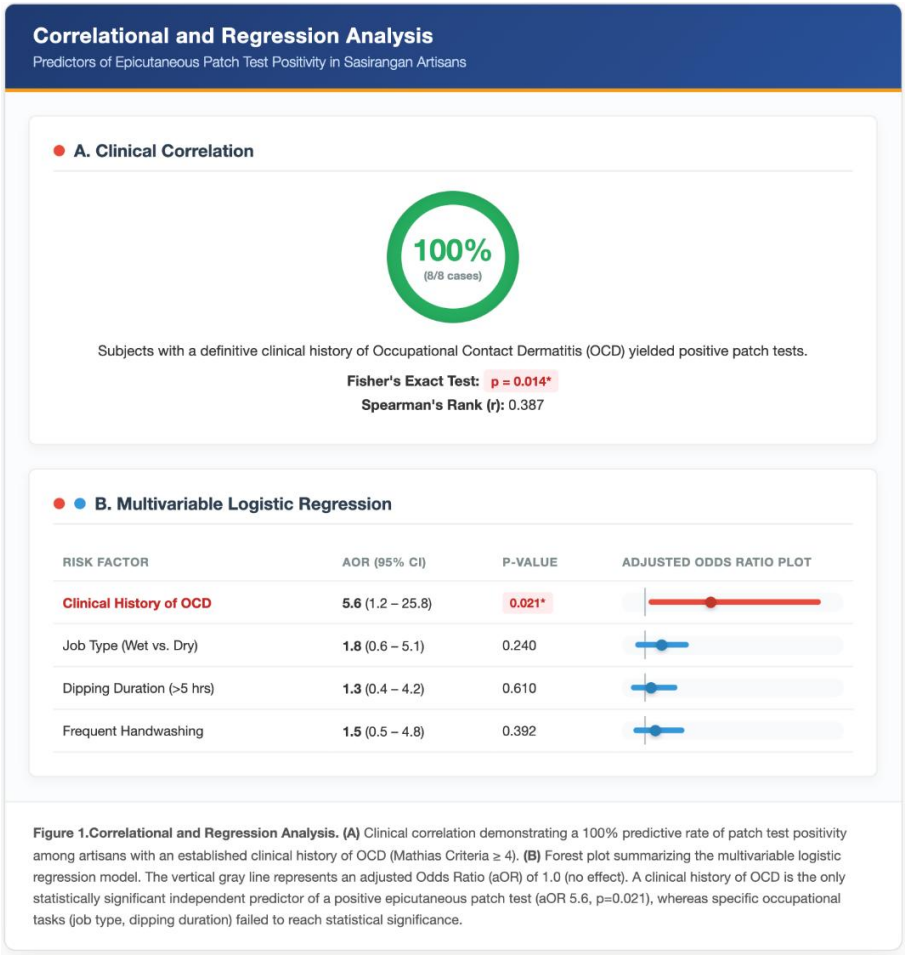

Figure 1.Correlational and Regression Analysis. (A) Clinical correlation demonstrating a 100% predictive rate of patch test positivity among artisans with an established clinical history of OCD (Mathias Criteria ≥ 4). **(B)** Forest plot summarizing the multivariable logistic regression model. The vertical gray line represents an adjusted Odds Ratio (aOR) of 1.0 (no effect). A clinical history of OCD is the only statistically significant independent predictor of a positive epicutaneous patch test (aOR 5.6, p=0.021), whereas specific occupational tasks (job type, dipping duration) failed to reach statistical significance.

4. Discussion

The remarkably high 62.5 percent prevalence of positive epicutaneous patch tests among the traditional Sasirangan artisan cohort represents an exceptionally severe burden of occupational sensitization. To contextualize the magnitude of this finding, general population averages for clinically significant hand eczema and allergic contact dermatitis typically range between 5 and 15 percent. Even within recognized high-risk industrial occupations, such as hairdressing, metallurgy, and formal textile manufacturing, sensitization rates rarely exceed 30 to 40 percent. The magnitude of disease burden discovered in this informal artisan population is profound.[11] Historically, the global dermatotoxicological literature has heavily incriminated disperse dyes as the primary, and often exclusive, culprits of textile-related allergic contact dermatitis. Disperse dyes possess specific physicochemical properties—namely, an exceedingly low molecular weight, profound lipophilicity, and weak, non-covalent fiber-binding characteristics—that allow them to easily detach from fabrics, dissolve in human sebum, and seamlessly penetrate the intact stratum corneum to initiate an immune response. Our findings fundamentally pivot this firmly established toxicological paradigm. We have conclusively demonstrated that synthetic VAT dyes, specifically the formulations willanthrene brill rose 4R and willanthrene green B, do not act as benign coloring agents, but as highly aggressive, primary sensitizers capable of driving severe morbidity within this unique occupational ecosystem.[12]

Understanding precisely why VAT dyes cause such profound allergic contact dermatitis requires a comprehensive exploration into the synergistic pathophysiology of the traditional dyeing micro-environment and the intricacies of human immunology. VAT dyes are inherently complex, large-molecular-weight compounds that are naturally water-insoluble.[13] Theoretically, these molecules should possess exceedingly poor epidermal penetrance and, therefore, a negligible sensitizing potential. However, this assumption collapses when evaluating the harsh realities of the manufacturing process.

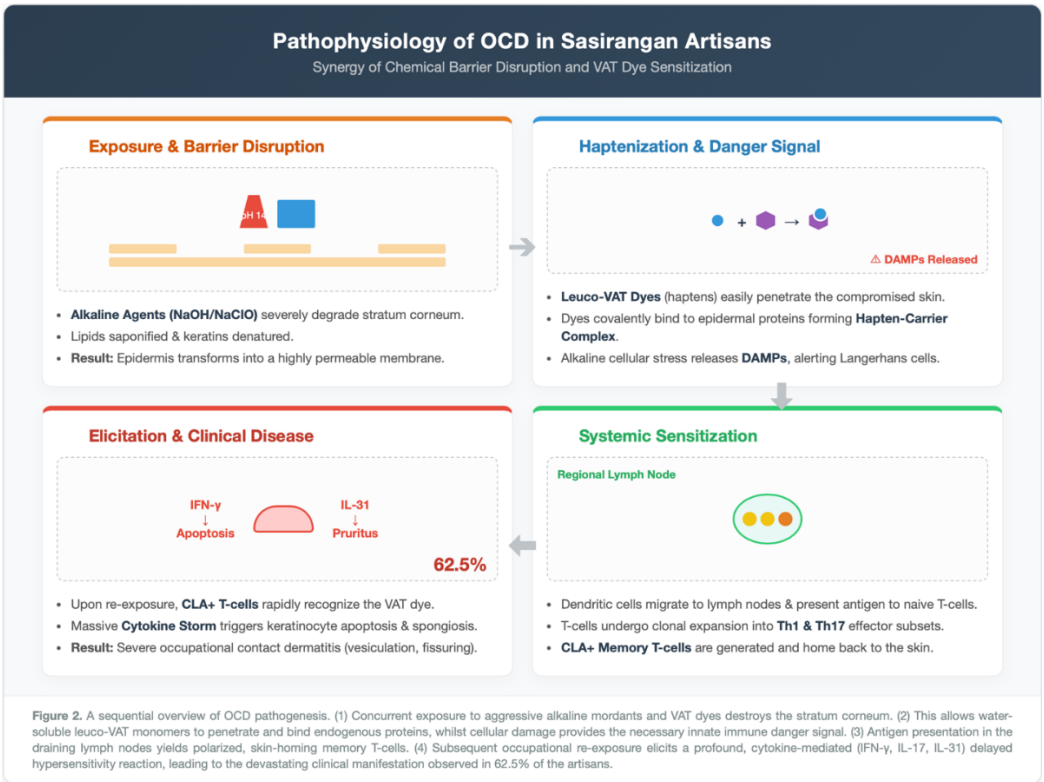

Figure 2. A sequential overview of OCD pathogenesis. (1) Concurrent exposure to aggressive alkaline mordants and VAT dyes destroys the stratum corneum. (2) This allows water-soluble leuco-VAT monomers to penetrate and bind endogenous proteins, whilst cellular damage provides the necessary innate immune danger signal. (3) Antigen presentation in the draining lymph nodes yields polarized, skin-homing memory T-cells. (4) Subsequent occupational re-exposure elicits a profound, cytokine-mediated (IFN-γ, IL-17, IL-31) delayed hypersensitivity reaction, leading to the devastating clinical manifestation observed in 62.5% of the artisans.

The initial stage of this pathological cascade is the Afferent Phase, encompassing massive barrier disruption and subsequent haptenization (Figure 2). Allergic contact dermatitis is a classic, textbook manifestation of a Type IV, cell-mediated delayed hypersensitivity reaction. The fundamental prerequisite for this reaction is that an exogenous chemical, termed a hapten, must successfully breach the outermost protective layer of the skin, the stratum corneum.[14] Because natural VAT dyes are insoluble, the Sasirangan manufacturing process requires them to undergo severe chemical reduction to become temporary, water-soluble leuco compounds capable of impregnating cellulose fibers. This essential reduction is achieved through the utilization of highly potent alkaline agents, predominantly boiling sodium hydroxide and concentrated sodium hypochlorite.

Our clinical data explicitly show that 37.5 percent of the wet workers exhibited severe, blistering irritant or allergic reactions directly correlated to sodium hydroxide exposure. The constant exposure to these extreme alkaline liquids acts as a relentless chemical assault on the epidermis. The high pH profoundly disrupts the delicate acid mantle of the skin, while simultaneously saponifying the essential epidermal surface lipids. This chemical degradation systematically denatures structural keratins and drastically depletes the crucial stratum corneum ceramides, cholesterol, and free fatty acids that form the protective mortar between the corneocyte bricks. This chemically induced barrier dysfunction precipitates a drastic, pathological increase in transepidermal water loss and transforms the ordinarily impermeable skin into a highly porous membrane.[15]

Once this critical epidermal fortress is breached, the low-molecular-weight, water-soluble leuco-VAT monomers, alongside their semi-oxidized anthraquinone and indigoid chemical derivatives, easily penetrate deeply into the viable, living layers of the epidermis. Because these synthetic dye molecules are highly electrophilic, they actively seek out and covalently bind to the nucleophilic amino acid residues, such as cysteine and lysine, present on endogenous epidermal proteins. This irreversible covalent bonding creates a completely novel, immunogenic structure known as the hapten-carrier protein complex, marking the completion of the haptenization process.

However, the mere presence of a foreign antigen is frequently insufficient to trigger a full systemic immune response; the immune system requires context to differentiate between harmless environmental exposures and genuine threats. This context is provided by the innate immune danger signal.[16] The simultaneous, severe chemical burn induced by the alkaline reducing agents does considerably more than merely break the physical cutaneous barrier. The resulting acute cellular stress and widespread necrosis of epidermal keratinocytes trigger the massive release of intracellular molecules into the extracellular space. These molecules, which include extracellular adenosine triphosphate, fragmented hyaluronic acid, and reactive oxygen species, act as Damage-Associated Molecular Patterns. These danger signals are rapidly detected by pattern recognition receptors, specifically Toll-Like Receptors 2 and 4, located on the surface of surviving keratinocytes and resident immune sentinels. The activation of these receptors triggers the assembly of the NLRP3 inflammasome within the cytoplasm, ultimately leading to the enzymatic cleavage of pro-interleukin-1 beta and pro-interleukin-18 into their highly active, pro-inflammatory states. This explosive cytokine release provides the critical Signal 2, the definitive danger signal absolutely required to initiate dendritic cell maturation and prevent immunological tolerance.

With the danger signal confirmed, the Sensitization and T-Cell Polarization phase begins. The resident epidermal Langerhans cells and deeper dermal dendritic cells rapidly engulf the foreign VAT dye-protein complexes. Upon activation by the inflammatory milieu, these specialized antigen-presenting cells downregulate their expression of E-cadherin, essentially detaching themselves from the

surrounding epithelial tissue matrix. Guided by specific chemokine gradients, particularly CCL19 and CCL21, they migrate through the afferent lymphatic vessels toward the regional draining lymph nodes. Upon arriving in the paracortical regions of the lymph nodes, these dendritic cells process the complex dye proteins into smaller peptide fragments and present them on their cell surface utilizing Major Histocompatibility Complex Class I and Class II molecules to naive T-cells.[17]

Driven by the highly specific cytokine environment generated by the dendritic cells, primarily interleukin-12 and interleukin-23, these naive T-cells undergo massive, rapid clonal expansion. They polarize into specialized effector memory subsets, predominantly T-helper 1 cells, which secrete interferon-gamma and tumor necrosis factor-alpha, and T-helper 17 cells, which secrete interleukin-17 and interleukin-22. Crucially, these newly minted, dye-specific memory T-cells upregulate a specific homing receptor known as cutaneous lymphocyte antigen. This receptor acts as a molecular zip code, allowing the memory cells to leave the lymph node, enter the systemic circulation, and selectively migrate back to the cutaneous tissues, where they take up silent residence, completely sensitizing the artisan to future exposures.

The final stage of this pathophysiological timeline is the Elicitation Phase, which corresponds directly to the devastating clinical manifestations observed in the artisan cohort. Upon subsequent re-exposure to the Sasirangan VAT dyes, the hapten once again penetrates the compromised epidermal barrier. It is immediately captured and presented to the resident, priming memory T-cells. Recognizing their specific antigen, these memory cells instantly degranulate, unleashing massive quantities of interferon-gamma and interleukin-17 into the surrounding tissue. Interferon-gamma powerfully stimulates local keratinocytes to express intercellular adhesion molecules and secrete additional chemokines, which rapidly recruit waves of inflammatory macrophages and highly destructive cytotoxic CD8 positive T-cells to the exact site of exposure. These cytotoxic T-cells induce widespread, localized keratinocyte apoptosis utilizing the Fas ligand and perforin-granzyme pathways. Microscopically, this massive cellular destruction presents as profound epidermal spongiosis and the accumulation of fluid, which clinically manifests as the debilitating intraepidermal vesiculation, blistering, and intense, burning erythema characteristic of the extreme positive patch test reactions observed in twenty-five percent of our affected cohort.[18] Furthermore, the concurrent release of the neuro-cytokine interleukin-31 drives the intense, unyielding pruritus that severely diminishes the artisans' quality of life.

Beyond the molecular mechanisms, the clinical correlations drawn from this study yield profound implications for occupational health management. A highly significant finding is the exceptional predictive power of a meticulously obtained clinical history of occupational contact dermatitis, yielding an adjusted odds ratio of 5.6. This unequivocally reaffirms the immense clinical validity of utilizing standardized, validated screening instruments, precisely like the Mathias criteria and the Nordic Occupational Skin Questionnaire, for early diagnostic screening. In resource-limited, informal industrial settings where highly specialized, expensive epicutaneous patch testing panels are logistically or financially entirely inaccessible, structured clinical anamnesis serves as a highly reliable, frontline prognostic tool to identify vulnerable workers before irreversible chronicity occurs.

Interestingly, the statistical analysis revealed no significant difference in patch test positivity rates between the wet workers, who demonstrated a fifty percent positivity rate, and the dry workers, who demonstrated a staggering seventy-five percent positivity rate. Traditionally, within the realm of occupational medicine, intense wet work—defined as continuous fluid immersion—is universally considered the paramount risk factor for contact dermatitis.[19] However, the unique micro-environment of Sasirangan manufacturing completely subverts this expectation. The dry workers, tasked primarily with

forcefully untying resist patterns, sewing, and ironing, are constantly manipulating semi-dry, heavily dye-saturated fabrics. The immense mechanical friction required to sever tight binding threads acts as a profound physical irritant, inducing micro-fissuring of the fingertips. Concurrently, the un-fixed, residual VAT dye dust becomes highly airborne in the poorly ventilated workspaces, settling onto the workers' skin and readily dissolving into their perspiration, effectively extracting the allergenic molecules directly into the compromised stratum corneum. This critical finding definitively proves that the profound occupational hazard is absolutely not confined solely to the highly visible wet dyeing vats but is insidiously pervasive throughout the entire lifecycle of textile production, threatening every individual within the facility.

Furthermore, the observation of polysensitization in an overwhelming sixty-eight percent of the positive cases highlights the deeply complex toxicological burden placed upon these workers. This phenomenon is highly likely attributable to the close structural homology shared between various synthetic anthraquinone-based VAT dyes and entirely distinct chemical families, such as azo-dyes. This structural similarity leads to profound immunological cross-reactivity at the T-cell receptor level, meaning a worker sensitized to one specific dye color will spontaneously develop severe allergic reactions to a multitude of distinct dyes, drastically compounding the clinical severity, chronicity, and therapeutic recalcitrance of their dermatitis.[20]

Naturally, the findings of this research must be contextualized within its inherent methodological limitations. The primary limitation resides in the restricted geographical and cultural scope of the investigation, focusing exclusively on a localized, albeit highly representative, artisan community in South Kalimantan. This localization may limit the broad global generalizability of the exact epidemiological prevalence rates to entirely different manufacturing practices. Furthermore, the cross-sectional, observational nature of the research design restricts the ability to definitively track the longitudinal trajectory of immunological sensitization over multiple decades of exposure. Additionally, the potential presence of the healthy worker survivor effect—where the most severely affected individuals systematically exit the profession prior to study enrollment—suggests that the remarkably high prevalence rates documented here might actually represent an underestimation of the true biological hazard. Future prospective, longitudinal cohort studies are imperative. These future endeavors should heavily integrate advanced biochemical techniques, utilizing high-performance liquid chromatography to precisely isolate and test completely pure VAT dye isomers, eliminating the confounding variables of industrial impurities, while simultaneously incorporating extensive genetic screening to evaluate the role of inherent skin barrier deficiencies, such as filaggrin mutations, in individual occupational susceptibility.

5. Conclusion

In conclusion, the traditional Sasirangan batik industry, while serving as a vital cultural and economic pillar, currently harbors a severe, vastly under-recognized occupational public health crisis. This extensive study definitively identifies complex synthetic VAT dyes, specifically the widely utilized willanthrene brill rose 4R and willanthrene green B formulations, as highly aggressive, potent primary sensitizers. This revelation fundamentally challenges the long-standing dermatological assumption that disperse dyes hold exclusive responsibility for textile-induced allergic contact dermatitis. The profound, chemically induced destruction of the essential epidermal barrier by highly caustic alkaline mordants provides the exact necessary mechanism enabling these massive dye molecules to penetrate the skin and elicit intense, cell-mediated Type IV hypersensitivity reactions. The data unequivocally prove that a structured, validated clinical history remains a phenomenally powerful, statistically significant predictor of underlying allergic sensitization, serving

as a crucial tool for occupational physicians. Addressing this silent epidemic demands immediate, comprehensively targeted, and culturally sensitive interventions. Public health initiatives must prioritize the urgent implementation and subsidized distribution of high-grade, chemically impervious barrier protection, coupled with extensive occupational health literacy campaigns. Ultimately, ensuring the sustainable future of this magnificent heritage craft necessitates an industry-wide transition toward the formulation and utilization of less alkaline, hypoallergenic dyeing alternatives, fundamentally safeguarding the irreplaceable health and longevity of the artisans who preserve this cultural legacy.

6. References

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