Local Crude House Dust Extracts as a Substitute for Standardized House Dust Mite Extracts in Allergy Diagnostic and Immunotherapy

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ABSTRACT

Allergic diseases are a significant global health issue commonly triggered by house dust mite (HDM) allergens. Standardized HDM extracts are currently widely used in allergen immunotherapy (AIT) and diagnostic tests. However, in several tropical regions, such as Indonesia, these standardized extracts were either expensive, difficult to obtain, or did not represent local allergen exposure. Previous studies examined crude house dust extracts (CHDE) derived from locally collected dust as a possible substitute because it reflected the complex allergenic and other composition of the local environment. Therefore, this study aimed to review the potential of Local Crude House Dust Extracts (LCHDE) as a regionally relevant substitute source of allergens for both diagnostic and therapeutic applications. LCHDE reflects real environmental exposure, including region-specific mite, fungal, and bacterial components, which could better represent local allergen profiles. LCHDE offered a promising, cost-effective, and contextually relevant option for allergy diagnosis in developing regions. However, its application in immunotherapy necessitated rigorous allergen profiling, and regional collaboration was crucial to establish CHDE suitable for clinical use.

Keywords: *Local Crude House Dust Extracts, House Dust Mite, Skin Prick Test, Allergen Extracts, Allergen Immunotherapy.*

INTRODUCTION

Allergic diseases are identified by the World Health Organization (WHO) as among the top three conditions that require prevention and control in the 21st century. These diseases are systemic conditions that can present as various local health challenges, leading to anaphylactic shock in extreme instances. Various allergic diseases, such as allergic rhinitis (AR), allergic asthma syndrome (AAS), atopic dermatitis (AD), food allergies (FA), and eczema, arise from intricate interplays between genetic and environmental factors.[1] Accurate identification of sensitizing allergens plays a significant role in the diagnosis and management of these conditions. Failure to correctly identify causative allergens can lead to ineffective treatment, poor disease control, and unnecessary avoidance strategies.[2]

The skin prick test (SPT) is the most widely used and reliable diagnostic tool for

detecting allergen-specific immunoglobulin E (IgE).[3] The accuracy and diagnostic value depend significantly on the quality, potency, and relevance of the allergen extracts used. Inappropriate or non-representative allergen extracts may lead to false-negative or misleading results, thereby affecting clinical decision-making.[4] In Indonesia, the majority of allergen extracts used in SPT were imported from other temperate areas, making them difficult to obtain. These imported extracts are typically standardized against non-tropical allergens, which may not reflect the environmental and biological conditions in tropical countries, such as Indonesia. Imported products are often expensive, not always available in Indonesia, and require specialized storage conditions, which restrict accessibility in many healthcare facilities. [5]

Indonesia has unique environmental conditions, and the composition of house dust allergens may differ significantly from those in temperate regions.[6] CHDE contain soluble components of mold, pollen, bacteria, animal dander, mite, food, and household chemicals [7] House Dust Mite (HDM) allergens are the primary and most common source and become a key trigger for allergies and asthma. The concentration and dominance can vary significantly based on geographic location (specifically, humidity), home characteristics, and the presence of other allergen sources.[8] The dominant HDM allergen sources include *Dermatophagoides pteronyssinus, Dermatophagoides farinae,* and *Blomia tropicalis*.[9] Consequently, HDM allergens, such as Der p 1, Der f 1, and Blo t 5, are expected to be the most prevalent and significant components in CHDE within Indonesian homes.

LCDHE has gained increasing attention as a potential substitute allergen source for both diagnostic and therapeutic purposes. CHDE contains a broader spectrum of allergens, including region-specific mite species.[10] These standardized extracts may not reflect the actual allergen exposure in the Indonesian environment due to variations in species and protein profiles. LCHDE may better reflect the actual allergen exposure of local populations, potentially enhancing diagnostic relevance and patient-specific accuracy. Therefore, this study aimed to evaluate the potential of local CHDE as a substitute for standardized HDM in Indonesian allergy diagnosis and immunotherapy.

COMPOSITION AND CHARACTERISTIC OF CHDE

CHDE is a non-standardized preparation derived from environmental dust collected from a specific geographic location. It contains a mixture of HDM allergens, fungi, bacteria, pet dander, and chemical matter (**Figure 1**).[11] The allergen profile varies by geography, humidity, housing type, and occupant behavior.[12] According to previous studies, nitrogenous proteins and bacterial molecules, such as beta-glucan and endotoxin, are present in CHDE.[13,14] HDM were found in large numbers within the house dust extracts.

Major Mite-Derived Allergens

The primary constituents of CHDE are proteins derived from HDM, particularly *Dermatophagoides pteronyssinus*, *D. farinae*, and *Blomia tropicalis* in tropical regions.[15] These may produce potent allergens, such as Der p 1, Der f 1 (cysteine proteases), and Der p 2, Der f 2 (lipid-binding proteins), thereby disrupting epithelial barriers and activating pattern-recognition receptors on dendritic and epithelial cells.[16,17] Furthermore, Der p 23 and Der p 5 have been recognized as clinically relevant components, often underrepresented in older standardized extracts.[18]

CHDE typically contains a mixture of these allergens, along with structurally related proteins from other mite species and domestic arthropods. Previously conducted comparative proteomic studies have shown that the total protein concentration in CHDE may reach 2 mg/mL, with 20–30% being allergenically active.[19,20] However, these concentrations vary widely depending on region, housing condition, humidity, and collection method.

Microbial and Fungal Constituents

A distinguishing feature of CHDE is the coexistence of microbial and fungal derivatives.

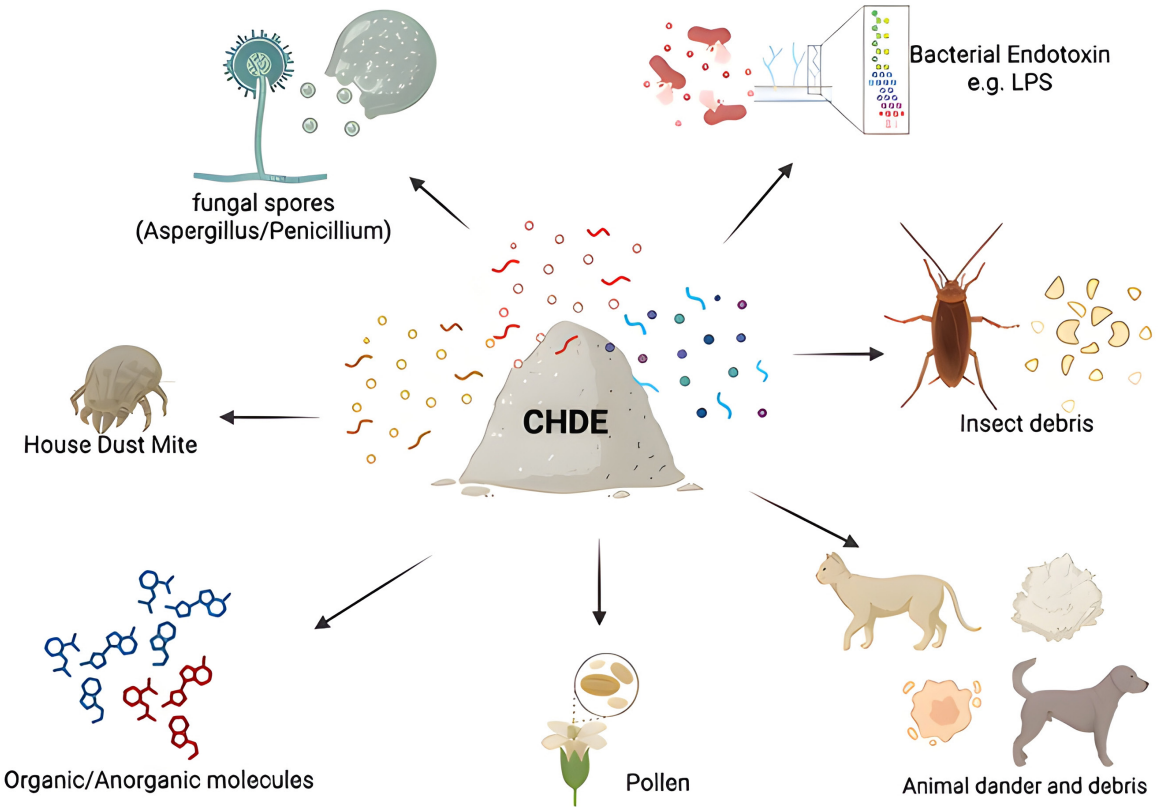

Figure 1. Composition of Crude House Dust Extract. CHDE contains a mixture of biological and non-biological components, including house dust mites, fungal spores (*Aspergillus, Penicillium*), bacterial endotoxins such as LPS, insect debris, animal dander, pollen, and various organic/anorganic molecules. Created with BioRender.com licensed by Odhi Anggani.

Indoor dust frequently contains Gram-negative bacterial endotoxins (lipopolysaccharides; LPS) and fungal β-glucans, which serve as potent innate immune adjuvants.[21] LPS can induce dendritic cell maturation through Toll-like receptor 4 (TLR4) signaling, thereby enhancing Th2-skewed immune responses when co-exposed with HDM allergens.[22] Fungal β-glucans and proteases from *Aspergillus*, *Penicillium*, and *Cladosporium* species also contribute to airway inflammation and epithelial damage.[23]

Endotoxin, a pro-inflammatory component of the outer membrane of Gram-negative bacteria, plays a significant role in the development and modulation of allergic disease by stimulating T helper type 2 responses while suppressing type 1 activity.[24] These endotoxins are potent immunological adjuvants that signal through Toll-like receptor 4 and help induce primary allergic immune responses. HDM extracts from household dust contain LPS, which contribute to the total inflammatory potential.[25] According to Arlian et al.,[26] the protein mixtures of LPS and HDM could change cytokine secretion patterns in human dermal fibroblasts, showing possible synergistic effects between microbial and allergic components within CHDE.

Insect and Domestic Animal Residues

CHDE frequently contains insect debris (cockroach and mosquito fragments) and animal-derived dander proteins, particularly in mixed-household environments. Cockroach allergens, such as Bla g 1 and 2, coexist with Der p 1, leading to cross-reactive sensitization patterns in individuals from tropical or high-density urban settings. Studies from Thailand and Indonesia have reported that more than 40% of household dust samples show combined mite–cockroach allergen signatures.[9,27]

Non-Protein Components and Chemical Irritants

CHDE contains a variety of non-protein molecules, such as lipids, detergents, and

environmental pollutants, adsorbed onto dust particles. Fatty acids and oxidized lipids from human skin and textiles can act as adjuvants, modulating allergen uptake and immune activation.[28] Trace levels of volatile organic compounds (VOCs), phthalates, and particulate matter may also be detected and synergize with biological allergens to exacerbate airway reactivity.[29]

The natural variability in the physicochemical properties of CHDE poses challenges to reproducibility. Similarly, it explains the complex and diverse factors in exposure to indoor allergens. Detailed analysis using SDS-PAGE, LC–MS/MS, and ELISA has shown that CHDE contains a wide range of protein components, typically between 10 and 100 kDa. According to a previous study, this range corresponds with the molecular weights of known mite and fungal allergens. [30]

Regional Variability and Environmental Influence

The composition of CHDE is highly influenced by geographic and climatic factors. *D. farinae* predominates in temperate areas, while *Blomia tropicalis* and *D. pteronyssinus* are more prevalent in tropical climates.[31] Studies conducted in Malaysia and Indonesia showed that high humidity (>70%) and year-round temperatures of 25–30 °C promote mite proliferation and increase Der p 1 concentrations in local dust samples.[32] However, homes with frequent cleaning and air conditioning exhibit lower allergen loads but increased microbial endotoxin diversity.[33] These results suggest that locally prepared CHDE show the true exposure patterns of each area. Consequently, locally prepared CHDE are a better diagnostic or study tool in endemic areas compared with imported standardized extracts, which lack specificity.

IMMUNOLOGICAL REACTIVITY AND MECHANISMS OF CHDE

CHDE elicits a broad spectrum of immune responses due to its complex composition, which includes allergenic proteins, microbial components, and proinflammatory mediators. Purified *Dermatophagoides* extracts primarily target IgE-mediated mechanisms, while CHDE activates both innate and adaptive immune pathways, showing the natural immunological milieu of environmental exposure.

IgE Binding and Cross-Reactivity

The diagnostic and immunologic relevance of CHDE largely depends on its ability to bind allergen-specific IgE from sensitized individuals. Comparative studies have shown that CHDE induces IgE reactivity similar to or slightly broader than standardized HDM extracts.[34] Immunoblot and ELISA analyses show that serum IgE from HDM-allergic patients recognizes multiple protein bands in CHDE corresponding to known mite allergens, including Der p 1, Der f 2, and Der p 23. Furthermore, this broad antigenic recognition shows CHDE's potential to capture the complexity of environmental allergen exposure. In areas where multiple allergen sources coexist, the broad reactivity could provide a more comprehensive reflection of local sensitization patterns.

Activation of Innate Immune Pathways

Beyond adaptive IgE responses, CHDE potently activates innate immune signaling. Epithelial cells exposed to CHDE upregulate alarmins, such as IL-25, IL-33, and thymic stromal lymphopoietin (TSLP), which subsequently prime dendritic cells (DCs) toward a Th2-polarizing phenotype.[35] The proteolytic activity of mite-derived enzymes (e.g., Der p 1) disrupts epithelial tight junctions, facilitating allergen penetration and activating protease-activated receptors (PAR-2). [36]

Microbial contaminants, including LPS and β-glucans, act synergistically with mite allergens to enhance DC activation through pattern recognition receptors, such as Toll-like receptors (TLR2, TLR4) and Dectin-1. This combined stimulation promotes the production of IL-6, IL-10, and IL-12p70, forming a cytokine milieu that favors Th2 and Th17 differentiation.[37] The integration of microbial signals distinguishes CHDE from purified extracts, which often lack the innate immune triggers.

Th2 Polarization and Cytokine Response

In animal and in vitro models, CHDE exposure induces robust Th2-type immune

responses characterized by increased secretion of IL-4, IL-5, and IL-13.[38]These cytokines stimulate IgE class switching in B cells, eosinophil recruitment, and mucus hypersecretion in airway epithelia. Studies comparing CHDE and standardized HDM extracts have shown comparable levels of Th2 cytokine production, though CHDE often elicits higher IL-17A and IL-33 expression due to its microbial components.[39] According to Moran et al.,[40] CHDE-conditioned pulmonary dendritic cells promoted potent Th2 differentiation against innocuous antigens, showing the presence of immunostimulatory activity.

Regulatory and Tolerogenic Responses

Although CHDE primarily drives allergic inflammation, some studies show that chronic or low-dose exposure can induce regulatory T-cell (Treg) expansion and IL-10 production, suggesting a dose-dependent modulation of the immune response. The presence of microbial products may activate tolerogenic dendritic cell subsets that suppress Th2 responses under certain exposure conditions. This dual potential-proinflammatory versus tolerogenic-depends on the relative concentrations of allergens, microbial ligands, and the host's immunogenetic background.[41] Understanding these dynamic responses is important in considering CHDE as diagnostic extracts and also a potential tool for allergen-specific immunotherapy (AIT), where immune tolerance induction is a desired outcome.

DIAGNOSTIC APPLICATIONS POTENTIAL OF CHDE

The diagnostic use of allergen extracts plays a fundamental role in identifying sensitization patterns and guiding clinical management of allergic diseases. Standardized HDM extracts, mainly *D. pteronyssinus* and *D. farinae,* are widely used in SPT, intradermal testing, and in vitro IgE assays. However, locally prepared CHDE are often used as substitutes in areas where standardized products are hard to obtain, limited, and expensive.

SPT remains the gold standard for evaluating immediate-type hypersensitivity reactions in allergic rhinitis, asthma, and atopic dermatitis.[42] Previous studies used CHDE as a diagnostic material in resource-limited settings or in early epidemiological surveys before the commercialization of standardized extracts.[34,43] Several studies have shown that CHDE can elicit positive SPT reactions in sensitized individuals, often correlating with symptoms of indoor allergy.[44] For example, LCHDE prepared from household dust in Malaysia showed SPT reactivity in more than 70% of patients with allergic rhinitis.[45] In comparison with standardized HDM extracts, the wheal diameters produced by CHDE are often larger and more variable due to the presence of nonspecific irritants or immunomodulatory molecules, such as endotoxin.

Serological assays for allergen-specific IgE (e.g., ELISA, ImmunoCAP) require well-characterized allergen preparations. Previous studies using house dust as antigenic material in IgE-binding assays have shown partial cross-reactivity with commercial HDM allergens. This result showed that house dust contains relevant IgE-binding proteins such as Der p 1, Der p 2, and Blo t 5.[46] The presence of additional non-mite proteins or microbial components in CHDE can lead to nonspecific binding. Furthermore, batch variability in house dust preparation affects test reproducibility. Even when the same house dust is used, variations in extraction methods, such as buffer pH, salt concentration, or filtration, can influence IgE-binding capacity.[47] These methodological differences may also affect the diversity and representation of allergens present in the CHDE, since house dust is a complex mixture containing multiple allergenic components.

Molecular allergology studies have shown that standardized HDM extracts predominantly contain defined allergens (Der p 1, Der p 2, Der f 1, Der f 2). Meanwhile, CHDE shows a broader environmental antigenic profile.[47] This may actually enhance ecological relevance in epidemiological surveys but reduces diagnostic precision in clinical settings.

IMMUNOTHERAPEUTIC POTENTIAL OF CHDE

AIT is the only disease-modifying treatment for IgE-mediated allergy. This treatment acts

through the induction of regulatory networks (Treg/IL-10), the generation of blocking IgG4 antibodies, and the progressive suppression of Th2 effector pathways. The majority of AIT products are manufactured from standardized, quantified allergen extracts to ensure potency and safety.[48] However, CHDE is an unrefined mixture of local mite allergens, fungal and bacterial components, animal proteins, and non-protein adjuvants (e.g., LPS, β-glucans). The theoretical rationale for using CHDE in AIT depends on two premises. The first is that CHDE better represents the real antigenic milieu to which patients are exposed, potentially improving ecological validity and cross-protection in polysensitized populations. In the second premise, microbial co-components may act as natural adjuvants that shape tolerogenic immune responses when delivered at appropriate doses.

CHDE may induce immune-modulatory mechanisms similar to those of standardized extracts. Desensitization is achieved by shifting from Th2-dominant inflammation to regulatory or Th1-biased immunity, characterized by elevated IL-10 and TGF-β secretion, suppression of IL-4 and IL-5, and increased allergen-specific IgG4.[49] According to a previous study, experimental murine models exposed to local HDM showed attenuation of airway hyperresponsiveness and reduced eosinophilic infiltration comparable to commercial mite extracts.[50] Furthermore, the presence of microbial-associated molecular patterns (MAMPs), such as LPS or β-glucan, in CHDE may engage innate Toll-like receptors, enhancing antigen presentation and immunological tolerance. [51]

The use of LCHDE for immunotherapy is a concept from the mid-20th century, predating the understanding of specific mite allergens and the technology for standardization. In Japan, house dust allergen extracts have been used for more than 40 years to treat HDM allergic rhinitis through subcutaneous immunotherapy (SCIT) and have been shown to be effective. Although CHDE contains mite allergens and other antigens, such as cockroach, moth, and mold, the Japanese Ministry of Health, Labour, and Welfare has approved its use for immunotherapy. [52]

High-quality evidence supports both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) as effective modalities for HDM allergy when standardized, potency-defined extracts are used. However, considering the diversity of allergen exposure across regions, CHDE provides an attractive conceptual advantage for regional representativeness and potential cost savings.

LIMITATION

Evidence supporting the clinical and immunotherapeutic use of CHDE remains limited and heterogeneous despite growing interest in region-specific allergen sources. Most studies used small sample sizes, variable extraction methods, and lacked references, leading to limited documentation. Studies about variability in dust composition, driven by regional differences in mite species, microbial flora, humidity, and altitude, can alter allergenic potency and immunogenic profile. Furthermore, the absence of standardized reference materials, potency units (e.g., Biological Allergy Units or mcg major allergen/mL), and validated bioassays for CHDE limits its reproducibility in diagnostic and therapeutic applications.

FUTURE DIRECTION

Advancing CHDE as a clinically acceptable substitute requires coordinated methodological, regulatory, and translational initiatives. First, standardization of extraction and quantification is essential, such as defining optimal solvents and protein stabilization systems (e.g., glycerol-based storage). Establishing *regional reference standards* through collaborative networks (ASEAN or Asia Pacific Allergy Consortium) could improve inter-laboratory reproducibility. Second, dose–response and safety evaluations should precede clinical application. Preclinical toxicity studies and in vitro immunoassays can determine safe allergen concentrations and endotoxin thresholds. Phase I/II clinical trials using CHDE for subcutaneous (SCIT) and sublingual (SLIT) immunotherapy should also be carried out under Good Clinical Practice (GCP) and GMP-like extracts preparation. Comparative non-inferiority designs against standardized

HDM AIT would provide a rigorous evaluation of clinical efficacy and safety. Third, integration of modern analytical technologies, such as mass spectrometry proteomics, next-generation sequencing of allergen transcripts, and endotoxin-specific biosensors, can define CHDE's molecular fingerprint and ensure batch consistency. Novel formulation method using nanoencapsulation or controlled-release adjuvants may further enhance the immunogenic stability of CHDE and reduce adverse reactivity. The establishment of regulatory frameworks for regional allergen extracts is necessary. Collaboration between national health authorities, academic institutions, and allergy societies ensures quality assurance while facilitating innovation in locally relevant diagnostic and immunotherapy products.

CONCLUSION

CHDE represents an intriguing, locally relevant allergen source with potential applications in allergy diagnosis and immunotherapy. Its complex composition shows real environmental exposure patterns, potentially providing a more comprehensive antigenic stimulus for immunomodulation. Although standardized HDM extracts remain the gold standard for AIT, CHDE serve as a region-specific option for both allergy diagnostic and immunotherapy, specifically in tropical and resource-limited areas where imported standardized extracts are costly or less representative. Realization of this potential depends on establishing controlled clinical evaluation and international harmonization of allergen quantification practices. Based on structured validation, CHDE may expand the accessibility and cultural relevance of allergen immunotherapy across the Asia–Pacific region or other tropical regions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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