Protocol for a scoping review on dermatophytes virulence factors: Bridging molecular understanding and research gaps

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Abstract

Background: Dermatophytoses are superficial skin mycoses caused by specialized keratinophilic filamentous fungi called dermatophytes,a group comprising various species that can infect humans and/or animals. With a global prevalence estimated at 25% of skin disorders and steadily increasing worldwide, dermatophyte infections represent a major public health concern. Given their widespread occurrence, zoonotic aspects, contagiousness, and emerging resistance to antifungals agents, elucidating the underlying mechanisms of dermatophyte infection has become essential. Current evidence indicates that dermatophyte pathogenicity involves a multistep infection process (adhesion, germination, and tissue invasion) driven by a complex arsenal of virulence factors. These include keratinolytic proteases, adhesion molecules, stress-response enzymes, secondary metabolites, and immune evasion mechanisms.

Aims: The objective of this scoping review is to synthesize current knowledge on virulence factors associated with dermatophytes (*Trichophyton*, *Microsporum*, *Nannizzia*, and *Epidermophyton* genera*)*, highlight key mechanisms involved in the infection process, and identify knowledge gaps that could guide future research and therapeutic innovation.

Materials and Methods: This scoping review, conducted according to the Joanna Briggs Institute methodology and PRISMA-ScR guidelines, will synthesize primary studies on virulence factors of dermatophytes. Experimental research (*in vitro*, *in vivo*, *ex vivo* and *in silico*) providing original data on molecular mechanisms or host–pathogen interactions will be included. Literature will be searched in Medline, CAB Abstracts, Scopus, Embase, and CINAHL, and screened independently by two reviewers in Covidence.

Conclusion: This review will offer a comprehensive summary of current data on dermatophyte virulence, thereby guiding future research directions and therapeutic innovation.

Keywords: Scoping review; dermatomycoses; dermatophytosis; dermatophytes; virulence factors; host–pathogen interactions; fungal skin infections; *Microsporum*; *Trichophyton*; *Epidermophyton*; *Nannizzia*.

Introduction

Dermatophytoses, commonly known as "ringworm" or "*tinea*", are superficial fungal infections of the skin with significant zoonotic potential. They are caused by keratinophilic filamentous fungi called dermatophytes, affecting both humans and animals (Weitzman and Summerbell, 1995). Among them, the genera *Trichophyton*, *Microsporum*, *Nannizzia*, and *Epidermophyton* include the species most frequently associated with these infections. In humans, dermatophytoses represent the most common fungal infections worldwide, with an estimated global prevalence accounting for approximately 20-25% of skin diseases, a figure that appears to be rising (Havlickova *et al*., 2008; Zhan and Liu, 2017). In parallel, the emergence of antifungal resistance in certain dermatophytes, such as *T. indotineae* has become a growing global concern (Verma *et al*., 2021; Al-Janabi *et al*., 2025).

The infection process typically involves three key stages: adhesion, germination and invasion. Initially, infectious arthroconidia adhere to the host's keratinized tissues through complex mechanisms involving specialized surface molecules (Esquenazi *et al*., 2003, 2004; Baldo *et al*., 2012) and secreted proteases (Baldo *et al*., 2008, 2010; Băguţ *et al*., 2012). Upon encountering favorable conditions, the arthroconidia germinate into hyphae capable of penetrating keratinized structures such as the stratum corneum, hair and nails (Liu *et al*., 2007). These hyphae can generate new arthroconidia, facilitating autoinoculation or transmission to new hosts, which contributes to the highly contagious nature of dermatophytoses.

Keratin degradation is a central pathogenic feature of dermatophytes (Grumbt *et al*., 2013), driven by a broad and complex arsenal of virulence factors, including keratinolytic proteases (Faway *et al*., 2025), stress-response enzymes (Carmo *et al*., 2022), adhesion molecules (Baldo *et al*., 2008), secondary metabolites (Kröber *et al*., 2016) and mechanisms of immune evasion (Huang *et al*., 2015). Despite increasing research interest, the molecular and cellular mechanisms underlying dermatophyte pathogenicity remain only partially characterized, and significant gaps persist in our understanding of host–pathogen interactions during infections.

The objective of this scoping review is to synthesize current knowledge on virulence factors associated with dermatophytes of the genera *Trichophyton*, *Microsporum*, *Nannizzia*, and *Epidermophyton*, to highlight key mechanisms involved in the infection process, and to identify knowledge gaps that may guide future research and therapeutic innovation.

Methods

This scoping review will be developed and conducted according to the Joanna Briggs Institute methodological framework for scoping reviews (Peters *et al*., 2024) and will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews checklist (PRISMA-ScR) (Tricco *et al*., 2018). The methodology, including search and study selection procedures, was iteratively developed and refined in collaboration with a health sciences librarian expert (SV) to ensure a comprehensive and targeted strategy.

Eligibility criteria

This scoping review will include published primary research articles addressing virulence factors of dermatophytes. Eligible study are those that identify or describe genes and/or proteins considered or demonstrated to act as virulence factors, including work exploring their molecular, biochemical, cellular or functional roles in pathogenicity. Studies may use *in vitro, in vivo*, *ex vivo* and *in silico* approach and may focus on any organism belonging to the genera *Trichophyton*, *Microsporum*, *Nannizzia* or *Epidermophyton*. No publication restrictions will be applied regarding country or region, and no publication date limits will be set. Only studies published in English will be included.

Studies will be excluded if they primarily address antifungal resistance rather than virulence, if they do not investigate virulence-related genes, proteins or mechanisms, or if they focus on other fungal genera or on mixed infections without specific data. Non-original research (such as narrative, systematic or scoping reviews), editorials, letters, opinion papers, conference abstracts, preprints, theses or other forms of grey literature, as well as books and book chapters, will also be excluded.

Search

The literature search was structured around two core concepts: "*dermatophytes and dermatophytosis"* and "*virulence factors"*. A comprehensive three-step search strategy was implemented to ensure systematic and exhaustive identification of relevant studies.

First, a preliminary search of Medline (via PubMed, from 1946) was conducted to identify relevant controlled vocabulary (MeSH terms) and free-text terms. Terms were extracted from key articles to inform the development of the final search strategy. Once the PubMed search equation was finalized,

its performance was assessed by verifying that a predefined set of key documents already identified by the authors was retrieved.

Second, the finalized search strategy was adapted for each of the following databases: CAB Abstracts (via EBSCOhost, from 1973), Scopus (via Elsevier, from 1974), Embase (via Elsevier, from 1974), and CINAHL (via EBSCOhost, from 1981). The complete search strategies for all databases are provided in **Appendix I**. For quality assurance, each database-specific query was validated by confirming its ability to retrieve a predefined set of five key articles already identified by the authors.

Third, the reference lists of all included sources of evidence will be screened manually to identify additional studies that may meet the inclusion criteria.

Selection of sources of evidence

Following completion of database searches, all identified records will be imported into Covidence (Veritas Health Innovation, Melbourne, Australia), where duplicates records will be automatically removed. Prior to the formal screening process, a pilot test was conducted on a sample of 35 records to ensure a shared understanding and consistent application of the predefined eligibility criteria by the review team. This pilot test was performed independently by two reviewers (RV and WP), and discrepancies were discussed and resolved to refine and standardize the study selection process.

Study selection will proceed in two sequential stages within Covidence, each conducted independently by the same two reviewers (RV and WP):

- screening of titles and abstracts
- full text screening of potentially eligible studies to determine final inclusion

Reasons for exclusion at the full-text screening stage will be documented for each study and reported in the final scoping review. Any disagreements between reviewers at any stage of the selection process will be resolved through discussion. If consensus cannot be reached, a third reviewer (BM) will be consulted.

The entire selection process, including the number of records identified, screened, included, and excluded (with reasons), will be documented and presented using a PRISMA flow diagram in the final report.

Data extraction process

Data from the included studies will be extracted independently by the two reviewers (RV and WP) using a data extraction form developed in Covidence. Following the pilot test described above, which encompassed both the study selection and date extraction procedures, the data extraction form was tested to assess its clarity, completeness, and consistency. Based on the results of this pilot test, the form was refined prior to full data extraction. The finalized date extraction form is provided in **Appendix II**.

Any discrepancies between the two reviewers will be resolved through discussion. If no consensus can be reached, a third reviewer (BM) will be consulted.

Data analysis and presentation

Results will be presented in tables and figures, accompanied by a narrative synthesis to provide additional context and insights into the body of literature.

Acknowledgements

Not applicable

Funding

This work was supported by the Walloon region, Walloon public service (*TineaDiag*, grant number 2410077)

Author contributions

Conceptualization: RV, WP, BM; Methodology: RV, WP, SV, BM; Data curation: RV, WP, BM; Investigation: RV, WP, BM; Writing – original draft: RV, WP, BM; Writing – review & editing: RV, WP, SV, BM; Visualization: RV, WP, BM; Supervision: SV, WP, BM; Funding acquisition: WP, BM.

Conflicts of interest

The authors state no conflict of interest.

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Appendices

Appendix I: Complete MEDLINE search strategy (*via* PubMed, 1946–Decembre 2025).

Concept		MEDLINE Search equation
#1	Dermatophytes and dermatophytosis	"Dermatomycoses"[Mesh] OR "Tinea"[Mesh] OR "Microsporum"[Mesh] OR "Trichophyton"[Mesh] OR "Arthrodermataceae"[Mesh] OR "Epidermophyton"[Mesh] OR "Onychomycosis"[Mesh] OR "athlete foot"[tiab:~3] OR "athletes foot"[tiab:~3] OR "dermatomycos*"[tiab] OR "dermatophytos*"[tiab] OR "epidermophytos*"[tiab] OR "jock itch*"[tiab] OR "kerion"[tiab] OR "microsporos*"[tiab] OR "nail fung*"[tiab] OR "onychomycos*"[tiab] OR "ringworm"[tiab] OR "sycosis"[tiab] OR "tinea*"[tiab] OR "trichophyto*"[tiab] OR "arthroderma*"[tiab] OR "ctenomyces"[tiab] OR "dermatophyte*"[tiab] OR "epidermophyton"[tiab] OR "keratinomyces"[tiab] OR "microsporum"[tiab] OR "nannizzia"[tiab]
AND		
#2	Virulence factors	"Virulence Factors"[Mesh] OR "Virulence"[Mesh] OR "Amidohydrolases"[Mesh] OR "Aminopeptidases"[Mesh] OR "Aspartic Acid Proteases"[Mesh] OR "Biomarkers"[Mesh] OR "Biofilms"[Mesh] OR "Carboxypeptidases"[Mesh] OR "Catalase"[Mesh] OR "Chitosan"[Mesh] OR "Dihydrolipoamide Dehydrogenase"[Mesh] OR "Dioxygenases"[Mesh] OR "Endopeptidases"[Mesh] OR "Glucans"[Mesh] OR "Glycoproteins"[Mesh] OR "Hemolysin Proteins"[Mesh] OR "Metalloproteases"[Mesh] OR "Peptide Hydrolases"[Mesh] OR "Phosphotransferases"[Mesh] OR "Polysaccharides"[Mesh] OR "Siderophores"[Mesh] OR "Subtilisins"[Mesh] OR "Sulfites"[Mesh] OR "Superoxide Dismutase"[Mesh] OR "Urease"[Mesh] OR "amidase*"[tiab] OR "amidohydrolase*"[tiab] OR "aminopeptidase*"[tiab] OR "aspartyl protease*"[tiab] OR "aspirochlorine*"[tiab] OR "biofilm"[tiab] OR "biological film"[tiab] OR "biological layer"[tiab] OR "biomarker*"[tiab] OR "carboxypeptidase*"[tiab] OR "catalase*"[tiab] OR "chitosan*"[tiab] OR "dehydrogenase*"[tiab] OR "deuterolysin*"[tiab] OR "dihydrolipoyl-dehydrogenase*"[tiab] OR "dihydrolipoamide dehydrogenase*"[tiab] OR "dioxygenase*"[tiab] OR "dipeptidylpeptidase*"[tiab] OR "elastase"[tiab] OR "endopeptidase*"[tiab] OR "fungalysin*"[tiab] OR "glucan*"[tiab] OR "glutam*"[tiab] OR "glycoprotein*"[tiab] OR "hemolysin*"[tiab] OR "hydrophobin*"[tiab] OR "keratinase*"[tiab] OR "kinase*"[tiab] OR "lipase*"[tiab] OR "mannan*"[tiab] OR "mannoprotein*"[tiab] OR "marker*"[tiab] OR "metallocarboxypeptidase*"[tiab] OR "metallopeptidase*"[tiab] OR "metalloprotease*"[tiab] OR "metalloproteinase*"[tiab] OR "pathogeni*"[tiab] OR "peptidase*"[tiab] OR "peroxidase*"[tiab] OR "peroxydase*"[tiab] OR "phosphotransferase*"[tiab] OR "polysaccharide*"[tiab] OR "proteinase*"[tiab] OR "protease*"[tiab] OR "secondary metaboli*"[tiab] OR "siderophor*"[tiab] OR "subtilisin*"[tiab] OR "sulfite*"[tiab] OR "superoxide dismutase*"[tiab] OR "urease*"[tiab] OR "viomellein"[tiab] OR "virulence"[tiab] OR "xanthomegnin*"[tiab] OR hydrolase*[tiab]
Number of records retrieved by the search		4,186 results

Appendix II: Complete data extraction template used in Covidence for the pilot test.

Heading 1	Heading 2	Heading 3	Responses
General information:	/	First autor's last name:	Free text
		Year of publication:	Free text
		Digital object identifier (DOI):	Free text
		Continent in which the study was conducted:	Structured options: • America • Australia • Africa • Europe • Asia • Other: free text
Characteristics of included studies:	Methods:	Aim of the study:	Free text
		Study design:	Structured options: • *In vitro* • *In vivo* • *Ex vivo* • *In silico* • Other: free text
		Declared conflicts of interest (if any):	Free text
	Organism characteristics and virulence factors investigated:	Genus of the dermatophyte:	Structured options: • *Trichophyton* • *Epidermophyton* • *Microsporum* • *Nannizzia*
		Host/experimental model:	Structured options: • Human • Rodent/rabbit • Horse • Cat/dog • Cattle • Other: free text

Virulence factors investigated:	/	Viruelnce factors investigated:	Structured options: • Adhesion factors • Biofilm / extracellular matrix • Hydrolases • Lipases • Oxidative stress protection mechanisms • Proteases • Kinases • Dehydrogenases • Secondary metabolites • Other: free text
		Method used to assess virulence factors:	Structured options: • Genomic analyses • Gene expression analyses • Protein detection and quantification, and protein-related or protein-mediated mechanisms • Other: free text
Other note:	Free text		