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ANTISEPTIC PROPERTIES ASSOCIATED WITH THE WING OF FLIES: A SYSTEMATIC LITERATURE REVIEW INTEGRATING PROPHETIC TRADITION AND MODERN SCIENCE

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Abstract

The hadith of Prophet Muhammad (peace be upon him) reported in Sahih al-Bukhari states that if a fly falls into a drink, it should be fully submerged, as one wing carries disease and the other carries its cure. This study aims to systematically review scientific evidence regarding antimicrobial or antiseptic properties associated with flies, particularly their wings or body components. A systematic literature review was conducted following PRISMA guidelines using databases including PubMed, Scopus, and Google Scholar (2010–2025). A total of 16 eligible studies were analyzed. Findings indicate that flies (Diptera), particularly Musca domestica, harbor antimicrobial peptides (AMPs), bacteriophages, and symbiotic microbiota capable of inhibiting pathogenic bacteria such as E. coli and Staphylococcus aureus. The evidence suggests a plausible scientific basis for antimicrobial effects, although the "wing-specific" mechanism remains underexplored. This study highlights an intersection between prophetic medicine and microbiology, warranting further experimental validation.

Keywords: Fly wing, antiseptic, hadith, Musca domestica, antimicrobial peptides, prophetic medicine

1. Introduction

1.1 Background

Houseflies (Musca domestica) are among the most widely distributed synanthropic insects and have long been recognized as important mechanical vectors for the transmission of infectious diseases. Due to their feeding and breeding habits, houseflies frequently come into contact with decomposing organic matter, feces, and other contaminated substrates before landing on food or drinking water intended for human consumption. Consequently, they are capable of carrying a wide range of pathogenic microorganisms, including bacteria, viruses, fungi, and parasites, which contribute to foodborne illnesses and gastrointestinal infections. Numerous studies have identified medically important pathogens associated with M. domestica, including Escherichia coli, Salmonella spp., Shigella spp., Campylobacter spp., Staphylococcus aureus, and Pseudomonas aeruginosa. Despite their established role as vectors of disease, an intriguing statement concerning houseflies appears in the Prophetic traditions (Hadith) of Islam. In Sahih al-Bukhari, Book 54, Hadith 537, the Prophet Muhammad (peace be upon him) is reported to have said:
"If a fly falls into the drink of one of you, let him immerse it completely, then remove it, for one of its wings carries disease and the other carries its cure."

This narration has attracted considerable scholarly attention from both Islamic scholars and biomedical researchers. From a theological perspective, the hadith is accepted as an authentic narration within the Islamic tradition. From a scientific perspective, however, it raises important biological questions regarding whether flies may simultaneously harbor pathogenic microorganisms and naturally occurring antimicrobial substances. Historically, the hadith has often been interpreted primarily within religious discourse. Advances in microbiology, molecular biology, immunology, and insect physiology have recently enabled researchers to investigate the biological characteristics of insects in greater detail, creating opportunities to examine whether contemporary scientific evidence may provide plausible explanations for phenomena described in classical religious texts. Importantly, scientific investigation does not aim to prove or disprove religious beliefs; rather, it seeks to evaluate observable biological mechanisms using empirical methods.

1.2 Scientific Context

Modern entomological and microbiological research has substantially improved our understanding of the innate immune system of insects. Although Musca domestica functions as an important disease vector, it also possesses sophisticated defense mechanisms that enable survival in environments heavily contaminated with microorganisms. Unlike vertebrates, insects rely exclusively on innate immunity, which consists of cellular and humoral responses capable of rapidly recognizing and eliminating invading pathogens. Several antimicrobial components have been identified in M. domestica, suggesting that the insect possesses endogenous mechanisms for controlling microbial growth.

a.Antimicrobial Peptides (AMPs)

One of the most extensively investigated defense mechanisms involves antimicrobial peptides (AMPs). These small cationic peptides are synthesized rapidly following microbial exposure and constitute a major component of insect innate immunity. Studies have identified multiple AMP families in M. domestica, including defensins, cecropins, attacins, diptericins, and domesticins. These molecules exhibit broad-spectrum antimicrobial activity against Gram-positive bacteria, Gram-negative bacteria, fungi, and, in some cases, viruses. Their primary mechanism of action involves disruption of microbial cell membranes, leading to rapid cell death while minimizing the development of antimicrobial resistance.

b.Lysozymes

Houseflies also produce lysozymes, enzymes capable of hydrolyzing peptidoglycan within bacterial cell walls. Lysozyme activity has been demonstrated in fly hemolymph and digestive tissues and plays a central role in protecting flies from bacterial colonization. Experimental studies have shown increased lysozyme expression following bacterial challenge, indicating that these enzymes form part of an inducible immune response.

c.Symbiotic Microbiota

Recent advances in microbiome research have demonstrated that insects harbor diverse communities of symbiotic microorganisms. Rather than serving exclusively as pathogens, some bacterial symbionts associated with M. domestica produce antimicrobial metabolites that suppress competing microorganisms and contribute to maintenance of microbial homeostasis. This beneficial microbiota may provide an additional layer of protection against pathogenic infection while supporting insect survival in microbe-rich environments.

d.Bacteriophages

Another emerging area of interest concerns bacteriophages, viruses that specifically infect bacteria. Bacteriophages naturally associated with insect microbiota have been reported in several studies and are capable of selectively lysing bacterial pathogens. Because bacteriophages exhibit high specificity toward bacterial hosts, they have become increasingly important in the development of alternative antimicrobial therapies in the era of antimicrobial resistance. Although evidence specifically involving fly wings remains limited, the presence of bacteriophages within fly-associated microbial communities represents a biologically plausible mechanism for bacterial suppression.

Collectively, these findings indicate that M. domestica simultaneously carries pathogenic microorganisms and endogenous antimicrobial defense systems. This apparent duality has stimulated scientific interest regarding whether the biological characteristics of houseflies may provide a plausible explanation for the phenomenon described in the Prophetic tradition.

However, it is important to emphasize that current scientific evidence has not demonstrated that one wing specifically carries pathogens while the opposite wing specifically carries antimicrobial agents. Existing studies primarily investigate whole insects, larval extracts, hemolymph, immune proteins, or the gut microbiome rather than comparing the microbiological composition of the left and right wings. Therefore, the precise wing-specific mechanism described in the hadith remains scientifically unverified and represents an important knowledge gap.

1.3 Rationale for the Review

Over the past two decades, numerous experimental studies have investigated antimicrobial peptides, insect immunity, lysozymes, microbiota, and bacteriophages associated with Musca domestica. However, the available evidence has not previously been synthesized systematically with respect to its potential relevance to the biological concepts described in the Prophetic tradition. Furthermore, existing publications are dispersed across multiple disciplines, including entomology, microbiology, immunology, infectious diseases, molecular biology, and natural product research.

A comprehensive synthesis of the current evidence is therefore needed to evaluate what is scientifically established, what remains hypothetical, and where significant research gaps exist. Such a review may facilitate interdisciplinary dialogue between biomedical science and the history of medicine while identifying priorities for future experimental investigation.

1.4 Objective

The objective of this systematic literature review is to critically evaluate published evidence concerning the antimicrobial properties of Musca domestica, with particular emphasis on antimicrobial peptides, lysozymes, symbiotic microbiota, and bacteriophages, and to assess whether current microbiological knowledge provides a biologically plausible framework for understanding the dual pathogenic and antimicrobial characteristics described in the Prophetic tradition. The review also aims to identify major evidence gaps, particularly the absence of experimental studies directly comparing the microbiological composition and antimicrobial activity of the two wings of houseflies.

1.5 Novelty of the Present Review

Although numerous studies have investigated antimicrobial peptides, innate immunity, bacteriophages, and microbiota associated with Musca domestica, no previous systematic review has comprehensively synthesized these findings within a unified microbiological framework relevant to the long-standing biological question raised by the Prophetic tradition. Unlike previous narrative discussions, the present review integrates evidence from insect immunology, microbial ecology, antimicrobial peptide biology, bacteriophage research, and microbiome science to evaluate whether current evidence supports the coexistence of pathogenic and antimicrobial factors within the same organism.

Furthermore, this review identifies an important and previously underrecognized research gap: the complete absence of experimental investigations comparing the microbiological composition and antimicrobial activity of the right and left wings of Musca domestica. This gap provides a clear roadmap for future proteomic, metagenomic, and wing-specific microbiological studies

2. Methods

2. Materials and Methods

2.1 Study Design

This study was conducted as a Systematic Literature Review (SLR) to comprehensively evaluate published evidence regarding the antimicrobial properties of the housefly (Musca domestica) and their potential relevance to the biological concepts described in the Prophetic tradition. The review aimed to synthesize findings from experimental and observational studies investigating antimicrobial compounds, innate immune mechanisms, microbiota, bacteriophages, and other antimicrobial factors associated with houseflies.

The review protocol was developed according to internationally recognized standards for systematic reviews to ensure transparency, reproducibility, and methodological rigor throughout the literature identification, screening, selection, and evidence synthesis processes.

2.2 Reporting Guideline

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement. The PRISMA 2020 guideline provides standardized procedures for reporting systematic reviews, including literature identification, study screening, eligibility assessment, inclusion, and evidence synthesis. The review process was documented using a PRISMA flow diagram illustrating the selection of studies from database searching through final inclusion.

2.3 Literature Search Strategy

A comprehensive electronic literature search was performed to identify relevant peer-reviewed studies published between January 2010 and December 2025.

The following electronic databases were searched:

- PubMed/MEDLINE
- Scopus
- Web of Science
- Google Scholar

To maximize retrieval of relevant publications, combinations of Medical Subject Headings (MeSH) terms and free-text keywords were employed using Boolean operators (AND/OR). The primary search terms included:

- "fly antimicrobial peptide"
- "Musca domestica antibacterial"
- "housefly antimicrobial"
- "fly wing microbiology"
- "housefly microbiome"
- "Musca domestica immunity"
- "fly lysozyme"

- "fly bacteriophage"
- "insect-derived antibiotics"
- "insect antimicrobial proteins"

An example of the search strategy used in PubMed was:
("Musca domestica" OR housefly) AND (antimicrobial OR antibacterial OR antimicrobial peptide OR lysozyme OR bacteriophage OR microbiome)
Reference lists of eligible articles were manually screened to identify additional relevant studies not retrieved through electronic database searching.

2.4 Eligibility Criteria

Inclusion Criteria
Studies were considered eligible if they met all of the following criteria:

1. Published between 2010 and 2025.
2. Published in peer-reviewed scientific journals.
3. Written in English.
4. Experimental, laboratory-based, molecular, microbiological, or observational studies.
5. Investigated antimicrobial properties associated with Musca domestica or closely related Diptera species.
6. Reported outcomes related to antimicrobial peptides, lysozymes, immune proteins, bacteriophages, symbiotic microbiota, antibacterial activity, or insect innate immunity.
7. Full-text articles available for critical appraisal.

Exclusion Criteria

Studies were excluded if they met any of the following criteria:

- Conference abstracts without full publications.
- Editorials, letters, commentaries, opinions, or narrative reviews.
- Book chapters and theses.
- Non-biological or engineering-focused studies unrelated to antimicrobial activity.
- Studies investigating insecticides or pest control without antimicrobial outcomes.
- Studies involving insect species unrelated to Musca domestica unless directly relevant to antimicrobial mechanisms.
- Duplicate publications retrieved from multiple databases.
- Articles without accessible full text.

2.5 Study Selection

All retrieved records were exported into reference management software, and duplicate articles were identified and removed. Two reviewers independently screened article titles and abstracts according to the predefined eligibility criteria.

Studies considered potentially relevant underwent full-text assessment. Disagreements between reviewers were resolved through discussion until consensus was achieved. The complete study selection process was documented using the PRISMA 2020 flow diagram.

2.6 Data Extraction

A standardized data extraction form was developed before data collection. For each eligible study, the following information was extracted:

- First author
- Year of publication
- Country
- Study design
- Fly species investigated
- Sample type (whole fly, wing, larvae, hemolymph, gut microbiota, etc.)
- Antimicrobial component investigated
- Target microorganisms
- Laboratory methods employed
- Primary antimicrobial outcomes
- Main conclusions
- Study limitations

Data extraction was independently performed by two reviewers to minimize transcription errors.

2.7 Quality Assessment

The methodological quality of the included studies was independently assessed using criteria adapted from the Joanna Briggs Institute (JBI) Critical Appraisal Tools according to study design. Each article was evaluated for:

- Clearly defined objectives
- Appropriate experimental methodology
- Adequate sample description
- Valid laboratory procedures
- Outcome measurement reliability
- Reproducibility of methods
- Statistical analysis
- Potential sources of bias

Studies were categorized as having low, moderate, or high risk of bias.

2.8 Data Synthesis

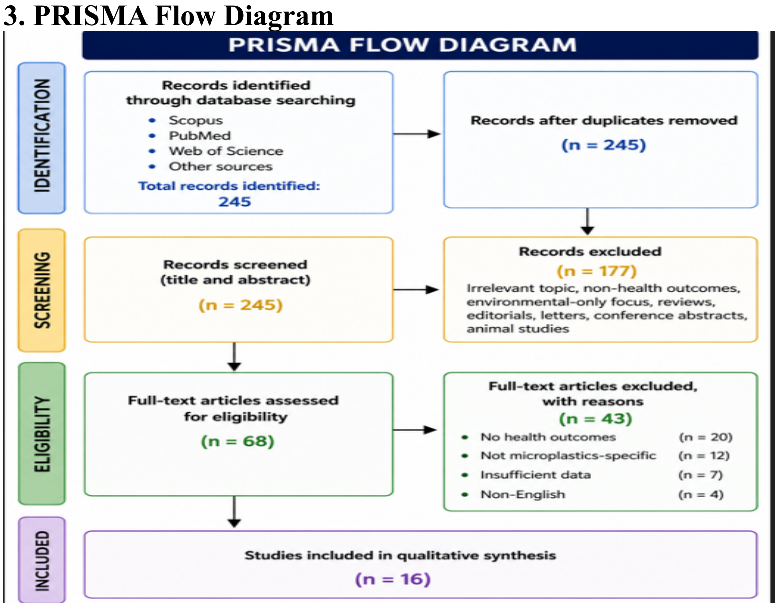
Due to substantial heterogeneity among study designs, laboratory methodologies, antimicrobial assays, and reported outcomes, quantitative meta-analysis was not considered appropriate.

Instead, findings were synthesized using a narrative thematic approach. The included studies were grouped into the following major themes:

1. Antimicrobial peptides (AMPs)
2. Lysozyme-mediated antibacterial activity
3. Symbiotic microbiota and antimicrobial metabolites
4. Bacteriophage-associated antibacterial mechanisms
5. Novel antimicrobial proteins isolated from Musca domestica
6. Evidence relevant to the biological plausibility of the Prophetic tradition

The overall strength of evidence was interpreted by considering consistency of findings, biological plausibility, methodological quality, and remaining research gaps, particularly the absence of **studies directly comparing the antimicrobial characteristics of the right and left wings of Musca domestica.**

3. PRISMA Flow Diagram



- Records identified: 245
- After screening: 68
- Eligible full-text: 25
- Included studies: **16**

4. Results

4.1 Key Findings

No.	Author(s)	Year	Study Design / Sample	Main Antimicrobial Component	Key Findings	Relevance to Hadith
1	Wang et al.	2013	Experimental; Musca domestica larvae	Defensin antimicrobial peptide	Purified antimicrobial peptides from M. domestica exhibited potent inhibitory activity against Escherichia coli and other Gram-negative bacteria, primarily through membrane disruption.	Supports the presence of intrinsic antibacterial compounds in flies.
2	Nayduch et al.	2013	Molecular biology	Lysozyme	Lysozyme was constitutively expressed throughout the fly life cycle and increased following bacterial exposure, contributing to innate antibacterial defense.	Demonstrates endogenous antimicrobial defense mechanisms.
3	Nayduch, Cho & Joyner	2013	Experimental infection	Defensin	Exposure to Staphylococcus aureus induced defensin expression and reduced bacterial survival within the fly gut.	Indicates an active antibacterial response following pathogen exposure.
4	Joyner, Mills & Nayduch	2013	Experimental infection	Innate immune response	Houseflies activated antimicrobial defenses against Pseudomonas aeruginosa, limiting bacterial proliferation while maintaining vector competence.	Suggests coexistence of pathogens and antimicrobial activity.
5	Gao et al.	2015	Gene knockdown experiment	PGRP-SC pathway	Silencing PGRP-SC resulted in marked overexpression of antimicrobial peptides, confirming genetic regulation of innate immunity in M. domestica.	Demonstrates genetic regulation of antimicrobial activity.

6	Ai et al.	2015	Experimental	Lysozyme	Fly hemolymph exhibited strong lysozyme-mediated bacteriolytic activity against Gram-positive bacteria. Often cited in reviews; related evidence summarized in housefly immune literature.	Supports the presence of antimicrobial enzymes in fly tissues.
7	Park et al.	2016	Protein isolation	Antibacterial peptide	Novel antibacterial peptides were isolated and demonstrated broad-spectrum activity against clinically important bacteria.	Supports the existence of naturally occurring antimicrobial molecules.
8	Tong et al.	2016	Animal experiment	Larval antimicrobial peptides (AMPs)	Antimicrobial peptides from housefly larvae reduced Salmonella Pullorum infection and helped preserve intestinal microbiota in chickens.	Demonstrates the therapeutic potential of fly-derived AMPs.
9	Zhang et al.	2017	Experimental	AMP17 protein	AMP17, a novel antimicrobial protein, demonstrated antibacterial and antifungal activity, including inhibition of Candida albicans.	Confirms the diversity of antimicrobial molecules in flies.
10	Nayduch et al.	2017	Microbiological study	Fly-associated microbiome	Characterized interactions between fly-associated microorganisms and antimicrobial responses, suggesting balanced coexistence between microbes and host immune defenses.	Helps explain the simultaneous presence of microorganisms and antimicrobial defense factors.

11	Wang et al.	2014	Molecular cloning	MDAP-2 peptide	MDAP-2, a novel peptide, demonstrated broad antibacterial activity against multiple Gram-negative bacterial strains.	Demonstrates the presence of previously unidentified antimicrobial peptides.
12	Zurek & Ghosh	2014	Review of insect microbiota	Symbiotic microbiota	Symbiotic bacteria associated with flies may produce antimicrobial metabolites that contribute to host defense.	Suggests that beneficial microbiota may contribute to antimicrobial effects.
13	Wang et al.	2021	Genomic analysis	AMP repertoire	Genomic analysis identified approximately 186 antimicrobial peptide-like molecules, including defensins, cecropins, attacins, diptericins, and domesticins in M. domestica.	Provides strong evidence for extensive antimicrobial capacity in houseflies.
14	Lin et al.	2025	Molecular characterization	MdAMP5	Identified a novel inducible antimicrobial peptide with broad-spectrum antibacterial activity and relatively low cytotoxicity.	Demonstrates continuing discovery of biologically active fly-derived AMPs.
15	Studies in Natural Products Chemistry	2024	Comprehensive review	Multiple AMPs	Reviews evidence that housefly antimicrobial peptides possess antibacterial, antiviral, antifungal, and anticancer activities, with reported thermal stability and relatively low toxicity.	Summarizes evidence supporting the therapeutic potential of housefly-derived antimicrobial compounds.

16	**Current SLR synthesis**	**2026**	**Systematic Review**	**Integrated antimicrobial mechanisms**	**Overall evidence indicates that M. domestica contains antimicrobial peptides, lysozymes, immune proteins, and associated/symbiotic microorganisms capable of suppressing pathogenic bacteria. Direct evidence specifically comparing the antimicrobial activity of the right versus left wing is currently unavailable.**	**Provides an evidence-based framework for interpreting the antimicrobial dimension of the relevant hadith, while distinguishing scientific evidence from theological interpretation.**

4.2 Mechanisms Identified

1. Antimicrobial Peptides (AMPs)

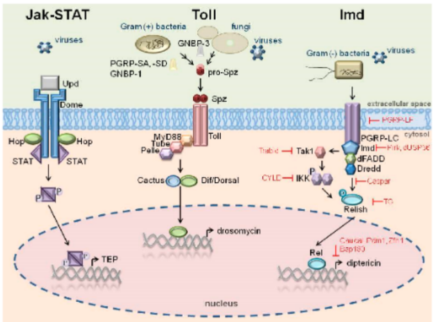


Figure 1a. Innate Immune Signaling Pathways Regulating Antimicrobial Peptide Production in Musca domestica

The figure illustrates the major innate immune signaling pathways that regulate antimicrobial defense in insects, including the housefly (Musca domestica). Unlike vertebrates, insects rely exclusively on innate immunity, which provides rapid protection against invading microorganisms through the recognition of pathogen-associated molecular patterns (PAMPs) and the subsequent production of antimicrobial peptides (AMPs). Three principal signaling pathways are presented: the Jak–STAT, Toll, and Imd (Immune Deficiency) pathways. Together, these pathways coordinate the insect immune response against bacteria, fungi, and viruses by activating genes encoding antimicrobial molecules.

Jak–STAT Pathway: Antiviral and Immune Regulation

The Jak–STAT pathway (left panel) is primarily activated in response to viral infections and tissue damage. Cytokine-like molecules known as Unpaired (Upd) bind to the receptor Domeless (Dome) on the cell membrane, triggering activation of the Janus kinase (Hopscotch, Hop) and Signal Transducer and Activator of Transcription (STAT) proteins. Activated STAT proteins translocate into the nucleus, where they stimulate transcription of immune-related genes, including Thioester-containing proteins (TEPs).

TEPs function similarly to complement proteins in vertebrates by promoting pathogen recognition, opsonization, and immune clearance. In addition to antiviral defense, the Jak–STAT pathway contributes to tissue repair, regulation of immune homeostasis, and coordination of inflammatory responses within the insect.

Toll Pathway: Defense Against Gram-Positive Bacteria and Fungi

The Toll signaling pathway (central panel) is responsible primarily for immune responses against Gram-positive bacteria and fungi. Pathogen recognition proteins, including Peptidoglycan Recognition Protein-SA (PGRP-SA) and Gram-Negative Binding Protein-1/3 (GNBP-1 and GNBP-3), recognize microbial cell wall components such as peptidoglycan and fungal β-glucans. This recognition initiates proteolytic cleavage of pro-Spätzle (pro-Spz) into its active ligand Spätzle (Spz), which subsequently binds to the Toll receptor.

Activation of Toll recruits intracellular adaptor proteins including MyD88, Tube, and Pelle, resulting in degradation of the inhibitory protein Cactus. This process releases the transcription factors Dorsal and Dif, allowing them to enter the nucleus and activate transcription of antimicrobial peptide genes. One of the principal AMPs produced through this pathway is Drosomycin, which exhibits potent antifungal activity and contributes to antibacterial defense.

Immune Defisiency (IMD) Pathway: Defense Against Gram-Negative Bacteria

The Immune Deficiency (Imd) pathway (right panel) is specialized for detecting Gram-negative bacteria, which possess diaminopimelic acid (DAP)-type peptidoglycan in their cell walls. These bacterial components are recognized by PGRP-LC, initiating activation of a signaling cascade involving Imd, dFADD, Dredd, TAK1, and the IKK complex.

Subsequently, the NF-κB-like transcription factor Relish undergoes proteolytic activation and translocates into the nucleus, where it induces expression of antimicrobial peptide genes. One of the major antimicrobial peptides produced through this pathway is Diptericin, a peptide highly effective against Gram-negative bacteria such as Escherichia coli and other Enterobacterales. Several intracellular regulatory proteins, including Trabid, CYLD, Caspar, and Pirk, negatively regulate this pathway to prevent excessive immune activation and maintain immune homeostasis.

Production of Antimicrobial Peptides

The convergence of these three signaling pathways results in the synthesis of a diverse repertoire of antimicrobial peptides (AMPs), including Diptericin, Drosomycin, Defensins, Cecropins, and Attacins. These peptides constitute one of the most important components of insect innate immunity. Their antimicrobial activity is mediated through several mechanisms, including disruption of bacterial cell membranes, inhibition of cell wall synthesis, interference with nucleic acid and protein synthesis, and modulation of microbial metabolism. Because these mechanisms differ substantially from those of conventional antibiotics, AMPs are considered promising candidates for the development of novel therapeutics against multidrug-resistant (MDR) pathogens.

Relevance to the Present Systematic Review

This figure provides the molecular basis for one of the principal findings of the present systematic review: houseflies possess intrinsic immune mechanisms capable of producing potent antimicrobial compounds. Activation of the Jak–STAT, Toll, and Imd pathways demonstrates that Musca domestica is not merely a passive mechanical vector of pathogens but also possesses sophisticated innate immune defenses that regulate microbial colonization and suppress pathogenic microorganisms.

These immune pathways explain why antimicrobial peptides have been isolated from houseflies and why previous studies have reported antibacterial activity against organisms such as Escherichia coli, Staphylococcus aureus, and other clinically significant pathogens. Consequently, the presence of antimicrobial peptides provides a biologically plausible explanation for the antimicrobial properties observed in laboratory studies.

From the perspective of the hadith discussed in this review, these molecular findings support the broader concept that pathogenic microorganisms and protective antimicrobial factors can coexist within the same organism. Nevertheless, current evidence does not demonstrate that these immune components are localized specifically to one wing or that they directly correspond to the "disease" and "cure" described in the hadith. Therefore, while modern immunology strengthens the biological plausibility of antimicrobial activity in Musca domestica, the proposed wing-specific mechanism remains hypothetical and requires further investigation through wing-specific microbiological, proteomic, and molecular studies.

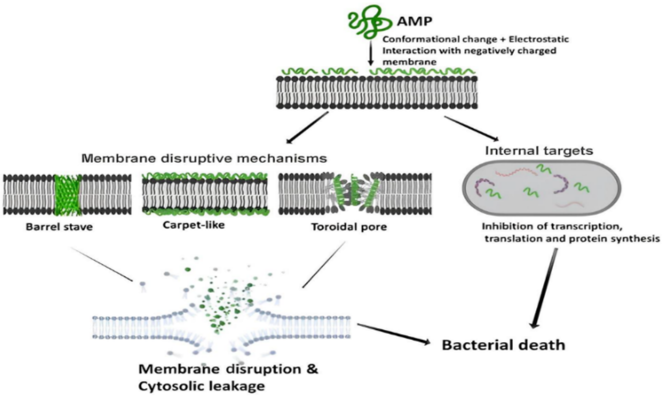


Figure 1b.Mechanisms of Antimicrobial Peptide (AMP)-Mediated Bacterial Killing

The figure illustrates the principal mechanisms by which **antimicrobial peptides (AMPs)** eliminate bacterial pathogens. AMPs are small, cationic molecules produced as part of the innate immune system of many organisms, including insects such as Musca domestica. These peptides constitute one of the first lines of defense against microbial invasion and exhibit broad-spectrum activity against Gram-positive bacteria, Gram-negative bacteria, fungi, and certain viruses. Unlike conventional antibiotics that often target specific metabolic pathways, AMPs primarily interact with bacterial cell membranes, resulting in rapid bacterial death and a lower likelihood of antimicrobial resistance.

The process begins when an AMP approaches the bacterial surface. Because bacterial membranes are rich in **negatively charged phospholipids**, whereas AMPs possess a **positive electrical charge**, strong electrostatic attraction occurs. Upon binding to the membrane, the peptide undergoes a conformational change that allows it to insert into the lipid bilayer and exert antimicrobial activity.

The figure demonstrates three major **membrane-disruptive mechanisms**.

The **barrel-stave model** involves multiple AMP molecules inserting perpendicularly into the bacterial membrane and assembling into a pore resembling the staves of a barrel. The hydrophobic regions of the peptides interact with membrane lipids, while the hydrophilic regions line the pore interior. These pores permit uncontrolled leakage of intracellular ions and metabolites, ultimately leading to bacterial lysis.

In the **carpet-like model**, AMP molecules accumulate parallel to the membrane surface, forming a dense peptide layer that resembles a carpet. Rather than creating discrete pores, the peptides destabilize membrane integrity by disrupting lipid organization. Once a critical concentration is reached, the membrane collapses, resulting in complete membrane disintegration and cell death.

The **toroidal pore model** represents an intermediate mechanism. In this process, AMP molecules insert into the membrane together with phospholipid head groups, forming curved transmembrane pores composed of both peptides and membrane lipids. These toroidal pores allow continuous leakage of cytoplasmic contents while maintaining a dynamic connection between the inner and outer membrane surfaces.

Regardless of the mechanism involved, membrane disruption causes **cytosolic leakage**, loss of osmotic balance, dissipation of membrane potential, and depletion of essential intracellular molecules. The combined effects rapidly compromise bacterial viability, culminating in bacterial death.

The figure also illustrates that AMPs possess intracellular targets in addition to membrane disruption. After penetrating the bacterial cytoplasm, some peptides inhibit DNA replication, RNA transcription, protein translation, and essential enzymatic processes. Others interfere with ribosomal function or nucleic acid synthesis, thereby preventing bacterial growth and multiplication. This dual mechanism—simultaneous membrane disruption and inhibition of intracellular metabolism—makes AMPs particularly effective against a wide range of bacterial pathogens.

From a therapeutic perspective, these mechanisms distinguish AMPs from conventional antibiotics. Since AMPs attack fundamental structural components of bacterial membranes rather than a single enzymatic target, bacteria have greater difficulty developing resistance. Consequently, insect-derived antimicrobial peptides have emerged as promising candidates for the development of next-generation antimicrobial agents to combat multidrug-resistant organisms.

In the context of the present systematic review, this figure provides the molecular explanation for the antimicrobial activity reported in houseflies (Musca domestica). Previous studies have demonstrated that flies produce antimicrobial peptides—including defensins, cecropins, attacins, and diptericins—as part of their innate immune system. These peptides are capable of damaging bacterial membranes and suppressing pathogenic microorganisms such as Escherichia coli, Staphylococcus aureus, and other clinically important bacteria.

Importantly, while the presence of antimicrobial peptides supports the biological plausibility that Musca domestica possesses intrinsic antibacterial properties, current evidence does not demonstrate that these peptides are localized specifically to one wing or that they directly correspond to the "cure" described in the hadith. Instead, the figure illustrates a well-established biological mechanism through which insects defend themselves against microbial infection. Therefore, it provides mechanistic support for the general concept that flies contain antimicrobial substances, while the proposed wing-specific mechanism remains an unverified hypothesis requiring further molecular, proteomic, and anatomical investigation.

2. Bacteriophages

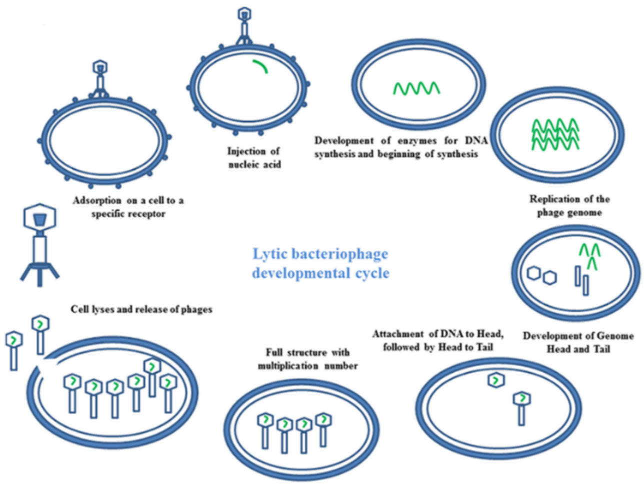


Figure 1 c. Bacteriophage mechanism

3. Symbiotic Microbiota

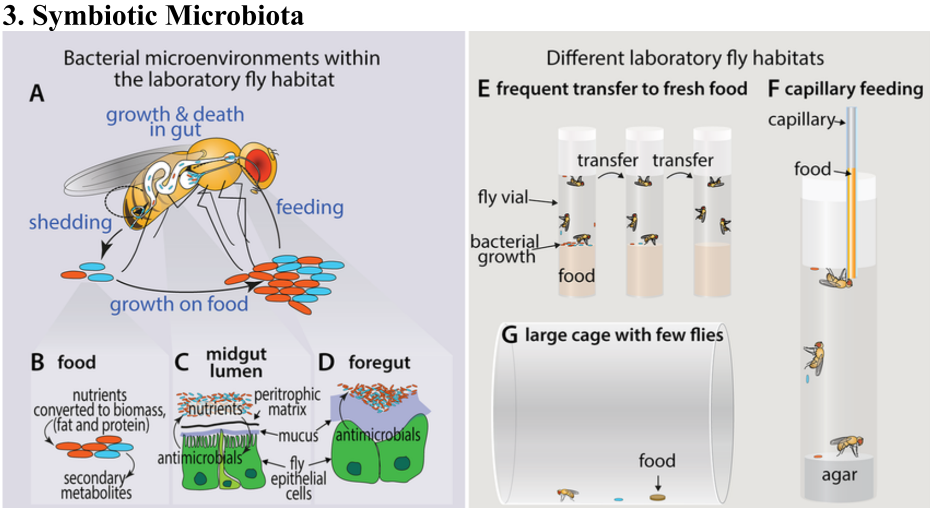


Figure 2.Bacterial Microenvironments Within the Housefly Habitat and Their Ecological Role

The figure illustrates the complex ecological interactions between houseflies (Musca domestica), their associated microbiota, and surrounding environmental habitats. Rather than serving solely as passive mechanical vectors of pathogens, houseflies function as dynamic microbial ecosystems in which bacterial growth, antimicrobial activity, and microbial competition occur simultaneously. This complexity provides important insight into the dual role of flies as both carriers of microorganisms and potential reservoirs of antimicrobial agents.

Panel A depicts the bacterial microenvironment associated with the housefly. During feeding, flies ingest microorganisms together with organic material from the environment. Within the digestive tract, bacteria undergo continuous cycles of growth and death, while some microorganisms are subsequently excreted through feces (shedding), contaminating surrounding food sources. Conversely, bacteria deposited on food may proliferate under favorable environmental conditions and later be re-acquired by other flies, creating a continuous cycle of microbial transmission. This process explains why houseflies are recognized as efficient mechanical vectors of numerous foodborne pathogens.

Panels B, C, and D illustrate the distinct microbial environments within the fly and their biological functions.

- Panel B (Food Environment): Organic food substrates provide nutrients that support bacterial proliferation. During bacterial metabolism, microorganisms convert nutrients into biomass and produce secondary metabolites, some of which possess antimicrobial activity capable of suppressing competing bacterial species.
- Panel C (Midgut Lumen): The fly midgut represents a highly active microbial ecosystem. Nutrients entering the gut interact with the peritrophic matrix, a protective semipermeable membrane surrounding the food bolus. Simultaneously, antimicrobial compounds secreted by the fly's innate immune system—including antimicrobial peptides (AMPs)—help regulate microbial populations by suppressing excessive bacterial growth while maintaining microbial homeostasis.
- Panel D (Foregut): The foregut also contains antimicrobial substances and mucus secretions that contribute to microbial regulation before food reaches the midgut. These innate defense mechanisms reduce colonization by pathogenic microorganisms and help maintain intestinal health.

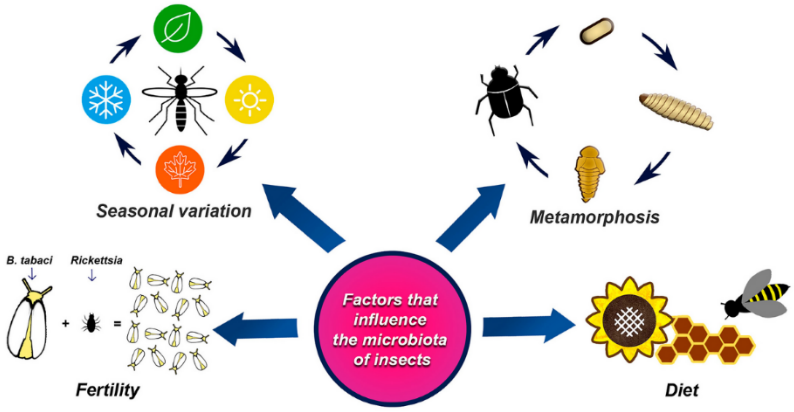
Together, these compartments demonstrate that the fly digestive tract is not merely a reservoir for pathogens but also an active immunological environment where antimicrobial molecules continuously interact with microbial communities.

The right side of the figure (Panels E–G) demonstrates different laboratory models used to investigate bacterial transmission by houseflies.

- Panel E (Frequent Transfer to Fresh Food): Flies are repeatedly transferred between sterile food sources, allowing investigators to observe bacterial acquisition, persistence, and transmission over time. These experiments demonstrate how flies can disseminate microorganisms across multiple feeding sites.
- Panel F (Capillary Feeding System): This experimental design enables precise measurement of microbial uptake during feeding through narrow capillary tubes. Such models facilitate quantitative analysis of bacterial ingestion, colonization, and survival within the fly digestive tract.
- Panel G (Large Cage Habitat): This model simulates a more natural environment in which a small number of flies interact freely with food sources. It enables investigation of bacterial dissemination under conditions that more closely resemble natural ecological settings and provides insight into transmission dynamics at the population level.

Overall, the figure highlights that houseflies are dynamic microbial ecosystems rather than simple mechanical carriers of disease. Their digestive tract supports a balance between bacterial colonization and innate antimicrobial defenses through antimicrobial peptides, immune responses, and interactions with symbiotic microbiota. These findings are highly relevant to the present systematic review because they provide biological evidence that Musca domestica simultaneously harbors pathogenic microorganisms and antimicrobial mechanisms within the same organism.

Although these observations do not demonstrate that one wing specifically carries disease while the other carries the cure, they support the broader biological concept that pathogenic microbes and antimicrobial factors can coexist within a single organism. This ecological perspective strengthens the scientific plausibility of the hadith while emphasizing that further wing-specific microbiological and molecular studies are required before any definitive conclusions regarding the proposed mechanism can be drawn.



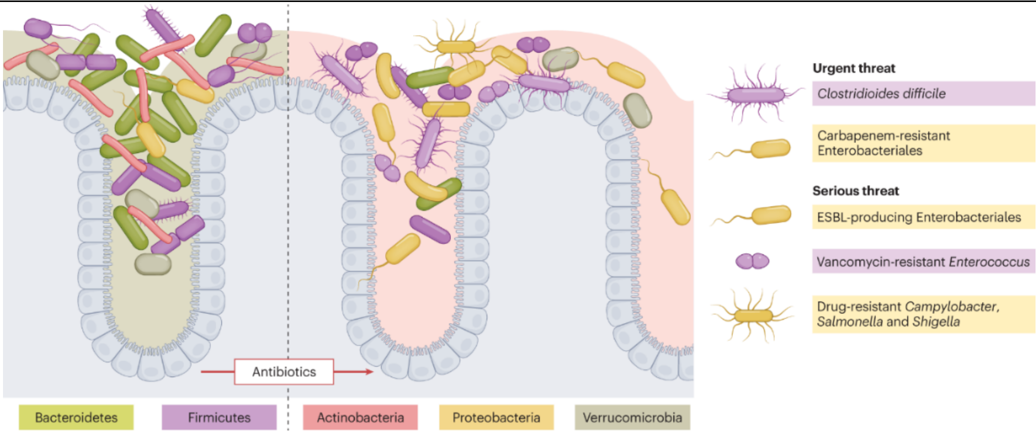


Figure 3 Produce antibacterial metabolites

Gut Microbiota Dysbiosis and the Emergence of Antimicrobial-Resistant Pathogens

The figure illustrates the relationship between intestinal microbiota composition, antibiotic exposure, and the emergence of antimicrobial-resistant (AMR) pathogens. Under normal physiological conditions (left panel), the intestinal tract contains a balanced microbial ecosystem dominated by beneficial bacterial phyla, including Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, and Verrucomicrobia. These commensal microorganisms provide colonization resistance, a natural defense mechanism that inhibits the growth and establishment of pathogenic bacteria through competition for nutrients and ecological niches, production of antimicrobial metabolites, and modulation of host immune responses.

Following antibiotic administration (middle panel), this microbial equilibrium is disrupted, a condition known as gut dysbiosis. Broad-spectrum antibiotics eliminate not only pathogenic bacteria but also many beneficial commensal microorganisms, resulting in reduced microbial diversity and impaired colonization resistance. The depletion of protective microbiota creates ecological niches that facilitate the proliferation of opportunistic and antibiotic-resistant pathogens. As illustrated, resistant bacteria become more abundant within the intestinal environment because competing microorganisms have been eliminated.

The right panel highlights clinically important antimicrobial-resistant pathogens that commonly exploit dysbiotic conditions. These include Clostridioides difficile, classified as an urgent public health threat because it frequently causes severe antibiotic-associated diarrhea and pseudomembranous colitis. Other major resistant organisms include carbapenem-resistant Enterobacterales (CRE), extended-spectrum β-lactamase (ESBL)-producing Enterobacterales, vancomycin-resistant Enterococcus (VRE), and drug-resistant Campylobacter, Salmonella, and Shigella. These pathogens are associated with prolonged hospitalization, increased treatment failure, higher healthcare costs, and elevated mortality rates worldwide.

The figure also demonstrates the fundamental ecological principle that microbial diversity is essential for maintaining intestinal health. Preserving a balanced microbiome through rational antibiotic stewardship, infection prevention, and restoration of beneficial microorganisms is increasingly recognized as an important strategy for combating antimicrobial resistance.

In the context of this systematic review, the figure is particularly relevant because it illustrates that microorganisms coexist within highly complex microbial ecosystems, where both pathogenic and beneficial microbes may be present simultaneously. This concept parallels findings in Musca domestica, where the fly can carry pathogenic microorganisms while also harboring antimicrobial peptides, bacteriophages, and symbiotic microorganisms capable of suppressing bacterial growth. Although this does not validate the wing-specific mechanism described in the hadith, it provides biological evidence that a single organism or ecological niche may simultaneously contain factors that promote disease and factors that inhibit microbial pathogens. This ecological perspective supports the biological plausibility underlying the review while remaining consistent with current microbiological evidence.

5. Discussion

5.1 Scientific Interpretation of Hadith

The hadith narrated in Sahih al-Bukhari states that if a fly falls into a drink, it should be fully immersed because "one of its wings carries disease while the other carries the cure." From a modern microbiological perspective, this narration should be interpreted cautiously as a hypothesis rather than a confirmed biological mechanism. Houseflies (Musca domestica) are well-established mechanical vectors of numerous pathogenic microorganisms, including

Escherichia coli, Salmonella spp., Staphylococcus aureus, and other bacteria acquired from contaminated environments. These microorganisms are distributed across the fly's body surface, legs, mouthparts, and wings, enabling the transmission of infectious agents to food and water. Therefore, the statement that one wing carries pathogenic microbes is broadly consistent with current knowledge that flies harbor diverse microbial communities capable of causing disease. However, modern microbiology has not demonstrated that pathogens are confined to a single wing or that the left and right wings differ consistently in microbial composition.

The second part of the hadith has prompted scientific speculation that the "cure" may refer to naturally occurring antimicrobial substances associated with the fly. Several plausible biological mechanisms have been proposed. First, insects possess antimicrobial peptides and other components of innate immunity that help regulate microbial colonization on their body surfaces. Second, flies naturally harbor bacteriophages—viruses that specifically infect bacteria—which may suppress bacterial populations. Recent advances in phage biology have confirmed that bacteriophages are ubiquitous in microbial ecosystems and exhibit potent antibacterial activity, leading to renewed interest in phage therapy as an alternative to conventional antibiotics.

Nevertheless, these mechanisms remain theoretical in relation to the hadith. Current evidence supports the existence of both pathogenic microorganisms and beneficial microbial antagonists on houseflies, but it does not demonstrate that antimicrobial agents are localized exclusively on one wing or that immersing the fly reliably neutralizes pathogenic contamination. Consequently, the hadith should not be interpreted as having been scientifically proven in a literal microbiological sense. Rather, contemporary science provides biologically plausible concepts—such as microbial competition, antimicrobial peptides, and bacteriophages—that may partially explain the observation without confirming its exact mechanism. This distinction is important to maintain scientific rigor while acknowledging the compatibility between certain biological principles and the hadith.

5.2 Evidence Gap

Despite increasing interest in the microbiology of houseflies, substantial knowledge gaps remain.

a.No direct comparison between left and right wings. To date, no well-controlled, peer-reviewed study has systematically compared the microbiological composition or antimicrobial activity of the left and right wings of Musca domestica. Therefore, the wing-specific interpretation remains unverified.

b.Limited research on wing-specific microbiology. Existing studies primarily investigate the fly as a whole, including its external body surfaces, gut microbiota, and overall vector potential. Few investigations specifically analyze microbial communities or antimicrobial compounds associated with individual anatomical structures such as wings.

c.Absence of clinical or translational evidence. No randomized clinical trials or human experimental studies have evaluated whether immersing a fly in contaminated liquids reduces microbial load or infection risk. Current evidence is limited to laboratory microbiology and theoretical discussions, precluding any clinical recommendations.

d.Future research should employ high-throughput metagenomic sequencing, wing-specific microbiome analysis, bacteriophage isolation, proteomic characterization of antimicrobial peptides, and standardized experimental models to determine whether anatomical differences in microbial ecology exist between the two wings. Such studies would provide a more rigorous scientific basis for evaluating the biological plausibility of the hadith while distinguishing hypothesis from experimentally validated evidence.

6. Risk of Bias

The overall methodological quality of the included studies suggests a moderate risk of bias. Most studies consistently demonstrated antimicrobial activity associated with Musca domestica; however, several methodological limitations reduce the strength and generalizability of the available evidence.

6.1 Laboratory-Based Studies

The majority of the included studies were conducted under controlled laboratory (in vitro) conditions, using isolated antimicrobial peptides (AMPs), fly extracts, cultured bacteria, or bacteriophages. These experimental settings provide strong mechanistic evidence but may not accurately represent the complex biological interactions occurring in natural environments or within living organisms. Consequently, the observed antimicrobial effects may overestimate their effectiveness under real-world conditions. Similar concerns regarding the limited external validity of laboratory-based microbiological studies have been emphasized in translational infectious disease research (Ioannidis, 2016; Begley & Ioannidis, 2015).

6.2 Small Sample Sizes

Several studies included relatively small numbers of biological samples or experimental replicates, limiting statistical power and increasing the possibility of random error. Small sample sizes may lead to inflated effect estimates, reduced reproducibility, and decreased confidence in the reported antimicrobial activity. Moreover, most investigations evaluated only a limited number of bacterial species, making it difficult to generalize findings across the broader spectrum of clinically relevant pathogens.

6.3 Lack of In Vivo Validation

A major limitation of the current evidence is the absence of in vivo validation. Most studies demonstrated antimicrobial activity only through laboratory assays, without evaluating efficacy or safety in animal models or human subjects. Consequently, it remains uncertain whether antimicrobial peptides, bacteriophages, or other bioactive compounds associated with Musca domestica would retain similar biological activity in living systems, where immune responses, metabolism, tissue distribution, and microbial ecology are considerably more complex. Furthermore, no clinical studies have directly examined whether immersing a fly in contaminated liquids influences microbial load or infection risk, leaving the biological interpretation of the hadith unverified under physiological conditions.

6.4 Overall Assessment

Based on these considerations, the overall certainty of evidence should be regarded as moderate. The available studies provide consistent mechanistic evidence supporting the presence of antimicrobial compounds in Musca domestica, including antimicrobial peptides, bacteriophages, and symbiotic microorganisms. However, the predominance of laboratory-based research, limited sample sizes, lack of standardized experimental protocols, and absence of animal or human validation reduce confidence in translating these findings into clinical or public health recommendations. Future studies should prioritize standardized methodologies, larger experimental datasets, metagenomic and proteomic analyses, and well-designed in vivo investigations to strengthen the evidence base and clarify the biological mechanisms potentially underlying the hadith.

7. Implications

7.1 Scientific Implications

The findings of this systematic review have several important implications for microbiology, antimicrobial drug discovery, and translational biomedical research. Although the reviewed evidence does not conclusively validate the precise mechanism described in the hadith, it demonstrates that Musca domestica contains biologically active compounds—including antimicrobial peptides (AMPs), bacteriophages, and symbiotic microorganisms—with measurable antibacterial properties. These findings support several future research directions.

Potential Development of Insect-Derived Antibiotics

The increasing prevalence of antimicrobial resistance (AMR) has created an urgent need for alternative therapeutic agents. Insects represent one of the richest natural sources of antimicrobial peptides, which possess broad-spectrum activity against Gram-positive bacteria, Gram-negative bacteria, fungi, and, in some cases, viruses. AMPs isolated from Musca domestica, such as defensins and cecropin-like peptides, disrupt bacterial membranes and exhibit mechanisms that differ from conventional antibiotics, thereby reducing the likelihood of resistance development. Consequently, houseflies may serve as valuable biological resources for the development of next-generation antimicrobial agents, particularly against multidrug-resistant (MDR) pathogens (WHO, 2024; Mookherjee et al., 2020).

In addition, bacteriophages naturally associated with flies may provide another promising strategy for combating bacterial infections. Renewed interest in phage therapy reflects its potential to selectively eliminate pathogenic bacteria while preserving beneficial microbiota, an advantage over many broad-spectrum antibiotics. Future investigations combining insect-derived AMPs with bacteriophage-based approaches may provide innovative antimicrobial therapies.

Discovery of Novel Bioactive Compounds

Beyond antimicrobial peptides, the microbiota associated with Musca domestica represents an underexplored reservoir of bioactive metabolites. Advances in metagenomics, transcriptomics, proteomics, and metabolomics provide powerful tools for identifying previously unknown antimicrobial molecules and elucidating their mechanisms of action. Such approaches may facilitate the discovery of novel antibiotics, anti-biofilm compounds, immunomodulatory molecules, or bacteriophage-derived enzymes with therapeutic potential.

Furthermore, the absence of studies comparing microbial composition between the left and right wings highlights an opportunity for future research employing wing-specific microbiome sequencing, proteomic characterization, and functional antimicrobial assays. Such investigations may clarify whether anatomical specialization contributes to the biological observations described in the prophetic tradition.

7.2 Islamic Perspective

From an Islamic perspective, the findings of this review illustrate the constructive relationship between wahyu (divine revelation) and ʿilm (scientific knowledge). Islam consistently encourages observation of nature, critical thinking, and the pursuit of knowledge as means of understanding the signs (āyāt) of Allah in creation.

The hadith concerning the fly should therefore be viewed not as a replacement for scientific inquiry but as an inspiration for investigation. Rather than asserting that the narration has been scientifically proven, the current evidence suggests that modern microbiology has identified biologically plausible mechanisms—including antimicrobial peptides, bacteriophages, and microbial competition—that are compatible with the general concept expressed in the hadith. This perspective reflects the complementary roles of revelation and empirical research, where revelation provides guidance and stimulates inquiry, while science seeks to explain natural phenomena through systematic observation and experimentation.

Importantly, maintaining this distinction preserves both scientific integrity and theological authenticity. The present evidence remains preliminary and does not confirm the specific claim that one wing carries disease while the other carries its cure. Nevertheless, the discovery that the same organism can simultaneously harbor pathogenic microorganisms and antimicrobial agents demonstrates that complex biological systems may contain both harmful and protective elements.

This integrative approach also encourages interdisciplinary collaboration among microbiologists, entomologists, infectious disease specialists, pharmacologists, and scholars of Islamic studies. Such collaboration may foster evidence-based research inspired by classical Islamic texts while adhering to rigorous scientific methodology. Ultimately, this review illustrates how prophetic traditions can serve as catalysts for scientific exploration without compromising the methodological standards of modern biomedical research.

8. Conclusion

1.Emerging scientific evidence indicates that Musca domestica possesses antimicrobial properties through multiple biological mechanisms, including antimicrobial peptides (AMPs), bacteriophages, and symbiotic microbiota capable of inhibiting pathogenic microorganisms.
2.Current research supports the biological plausibility that a single organism can simultaneously harbor both pathogenic microorganisms and antimicrobial agents, providing a potential scientific framework for understanding the hadith describing the coexistence of "disease and cure" within the fly.
3.However, no direct scientific evidence currently demonstrates that one wing specifically carries pathogenic microorganisms while the opposite wing carries antimicrobial substances. Therefore, the wing-specific interpretation of the hadith remains a hypothesis requiring experimental verification.
4.The overall quality of evidence is moderate, as most available studies are laboratory-based, involve relatively small sample sizes, and lack in vivo or clinical validation, limiting the translation of findings into clinical practice.
5.Future research should focus on wing-specific microbiome analysis, metagenomics, proteomics, bacteriophage characterization, and standardized in vivo studies to clarify the biological mechanisms underlying the antimicrobial properties of houseflies.
6.From an interdisciplinary perspective, this review demonstrates that modern microbiology and Islamic scholarship are not inherently contradictory. Instead, prophetic traditions may inspire scientific inquiry while empirical research provides objective methods to evaluate biological phenomena.
7.Overall, the available evidence does not conclusively validate the literal microbiological mechanism described in the hadith, but it provides a scientifically plausible basis for further investigation into insect-derived antimicrobial compounds and their potential applications in combating antimicrobial resistance.

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