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One Health Perspectives on Infectious Diseases, Environmental Biotechnology, and Novel Therapeutics

Venkatajothi Ramarao

Department of Microbiology, Saveetha Medical College and Hospital,
Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University,
Thandalam, Chennai - 602105, Tamil Nadu, India.

Correspondence author: Dr. Venkatajothi Ramarao

Address for correspondence: Department of Microbiology, Saveetha Medical College and
Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS),
Saveetha University, Thandalam, Chennai - 602105, Tamil Nadu, India.

Email id: drvjothi10@gmail.com

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Abstract

The One Health framework recognizes that human health, animal health, and environmental integrity are deeply and inseparably connected. Infectious diseases do not respect species boundaries or geographic borders, and the evidence accumulated over recent decades makes this abundantly clear. Zoonotic pathogens, antimicrobial resistant organisms, vector-borne diseases, and environmentally transmitted infections all emerge at the interface of human, animal, and ecosystem health, demanding integrated responses that no single discipline can provide alone. At the same time, biotechnology and the natural world are offering increasingly sophisticated tools for understanding and addressing these threats. Medicinal plants, microbial biotechnology, nanotechnology, and computational drug discovery are converging into a new therapeutic paradigm that draws on both traditional knowledge and cutting-edge science. This review explores One Health perspectives across interconnected domains including infectious disease epidemiology, antimicrobial resistance, environmental biotechnology, phytochemical therapeutics, vector-borne disease

management, and novel drug discovery strategies. By tracing these connections systematically, the review aims to highlight both the complexity of the challenges we face and the genuine promise of integrated, multidisciplinary solutions. The goal is not merely to catalog what is known but to illuminate the pathways through which science is moving toward more holistic and effective approaches to human and planetary health.

Keywords: Infectious diseases, One Health, antimicrobial resistance, *Boerhaavia diffusa*.

1. Introduction

There is something almost humbling about the One Health concept once you truly sit with it. The idea that a pathogen circulating in a bat population in a remote forest can, within months, become a global health emergency affecting billions of people is no longer hypothetical. It has happened, more than once, and the lessons have been painful and expensive [1, 2]. One Health is the formal recognition of something that ecologists, veterinarians, and public health specialists have long understood intuitively, that the health of humans cannot be meaningfully separated from the health of the animals they live alongside or the environments they inhabit [3, 4].

The infectious disease landscape has grown considerably more complex over the past few decades. Emerging and re-emerging pathogens, many of them zoonotic in origin, have repeatedly surprised health systems that were designed primarily to manage endemic diseases within fixed geographic boundaries [5, 6]. Bacterial infections that were once straightforward to treat have become progressively harder to manage as antimicrobial resistance spreads through human, animal, and environmental reservoirs simultaneously. The same antibiotics used in human medicine are used in veterinary practice and agriculture, creating selection pressures that operate across multiple ecosystems at once [7, 8].

Against this backdrop, the search for new therapeutic approaches has taken on genuine urgency. Medicinal plants have reentered the scientific conversation not as folklore but as a serious source of bioactive compounds with demonstrated activity against resistant pathogens and cancer cells [9, 10]. Researchers have documented meaningful antioxidant, antibacterial,

antifungal, and anticancer properties in plant species ranging from *Boerhaavia diffusa* to *Euphorbia hirta*, building an evidence base that supports further systematic investigation [11, 12]. These findings matter not just academically but practically, particularly in settings where access to conventional pharmaceuticals remains limited and plant-based remedies are already part of daily healthcare practice. Computational biology has simultaneously transformed how drug discovery works. Molecular docking, peptide design, and in silico screening have made it possible to evaluate thousands of candidate molecules against specific protein targets without ever running a single wet-lab experiment initially [13, 14]. This has dramatically compressed the early stages of drug discovery and opened up possibilities for repurposing existing approved drugs against new targets, including antimicrobial resistance proteins and cancer-associated receptors [15, 16]. The intersection of computation and natural product chemistry is producing genuinely novel leads that would have been extraordinarily difficult to identify through conventional screening alone.

Environmental biotechnology adds yet another dimension to this picture. The way human activities shape microbial communities in soil, water, and air has direct consequences for infectious disease emergence, antimicrobial resistance dissemination, and ecosystem resilience [17, 18]. Nanotechnology is beginning to offer tools for environmental remediation and pathogen detection that operate at levels of sensitivity and specificity previously unimaginable [19, 20]. Meanwhile, microbial biotechnology is finding productive applications in waste valorization, bioproduct synthesis, and sustainable agriculture that reduce environmental pressures driving disease emergence in the first place [21, 22].

This review brings these threads together through a One Health lens. It examines infectious disease epidemiology across human and animal populations, traces the environmental dimensions of antimicrobial resistance, surveys innovations in plant-based and computational therapeutics, and considers how nanotechnology and environmental biotechnology are reshaping both disease management and ecological health. The ambition is not simply to summarize but to show how these domains connect, reinforce each other, and collectively point toward a more integrated vision of health for people, animals, and the planet.

2. Infectious Disease Epidemiology in a One Health Context

Epidemiology looks different when you step back far enough to see the whole system. Individual cases of disease, which clinical medicine necessarily focuses on, are actually the visible tips of much larger ecological processes involving pathogen evolution, host population dynamics, environmental change, and human behavior [23, 24]. The One Health framework insists on this wider view, and the epidemiological evidence strongly supports it. Many of the most significant infectious disease challenges of our time are fundamentally ecological problems that happen to express themselves as human illness [25, 3].

Intestinal parasitic infections offer a compelling illustration of this point. Helminthic and protozoan infections remain stubbornly endemic across tropical and subtropical regions, particularly among school-aged children in communities where sanitation infrastructure is inadequate and environmental contamination of water and soil is common [26, 27]. Studies documenting the prevalence of intestinal helminths and protozoa among school children have consistently shown that infection rates reflect environmental conditions as much as individual behavior, with contaminated water sources, open defecation fields, and poor waste management serving as the primary transmission drivers [28, 7]. Treating infected children without addressing these environmental reservoirs

produces only temporary relief, as reinfection rates in endemic communities remain high.

Fungal infections present their own epidemiological complexity within a One Health context. *Tinea capitis* and oral candidiasis, both commonly encountered in pediatric populations, are shaped by environmental factors including humidity, crowding, and shared living conditions that influence fungal spore dispersal and host colonization [29, 30]. The antifungal sensitivity patterns of *Candida* isolates from school children have raised concerns about resistance development even in community settings, suggesting that antifungal use patterns in both human medicine and agriculture may be contributing to a shared resistance pool [11, 31]. This is a genuinely One Health problem, because the azole fungicides widely used in agriculture share mechanisms with the azole antifungals used clinically, creating cross-resistance dynamics that operate across environmental and clinical boundaries simultaneously.

Viral infections, particularly those involving oncogenic viruses like human papillomavirus, add further layers to the epidemiological picture. HPV transmission dynamics are shaped by behavioral, immunological, and social factors that intersect in complex ways, and the elevated prevalence of high-risk HPV types among HIV-positive women reflects how immunological vulnerability amplifies infection risk across multiple pathogen categories simultaneously [32, 33]. Understanding these co-infection dynamics is essential for designing screening and prevention programs that address multiple risks within single integrated interventions rather than treating each infection as an isolated clinical problem [34, 35].

Neurological complications of parasitic diseases represent one of the more severe manifestations of the One Health interface. Human African trypanosomiasis, caused by *Trypanosoma bruceirhodesiense*, illustrates how zoonotic pathogens transmitted through animal reservoirs and insect vectors can produce devastating neurological consequences in human hosts [36, 37]. Studies examining seizure prevalence in

stage-two rhodesiense trypanosomiasis have highlighted the profound neurological burden of this disease and the diagnostic and therapeutic challenges it poses in resource-limited settings where the animal reservoir, the tsetse fly vector, and the human host all share the same ecological space [38, 23]. Addressing this disease requires simultaneous attention to animal reservoir management, vector control, and human clinical care.

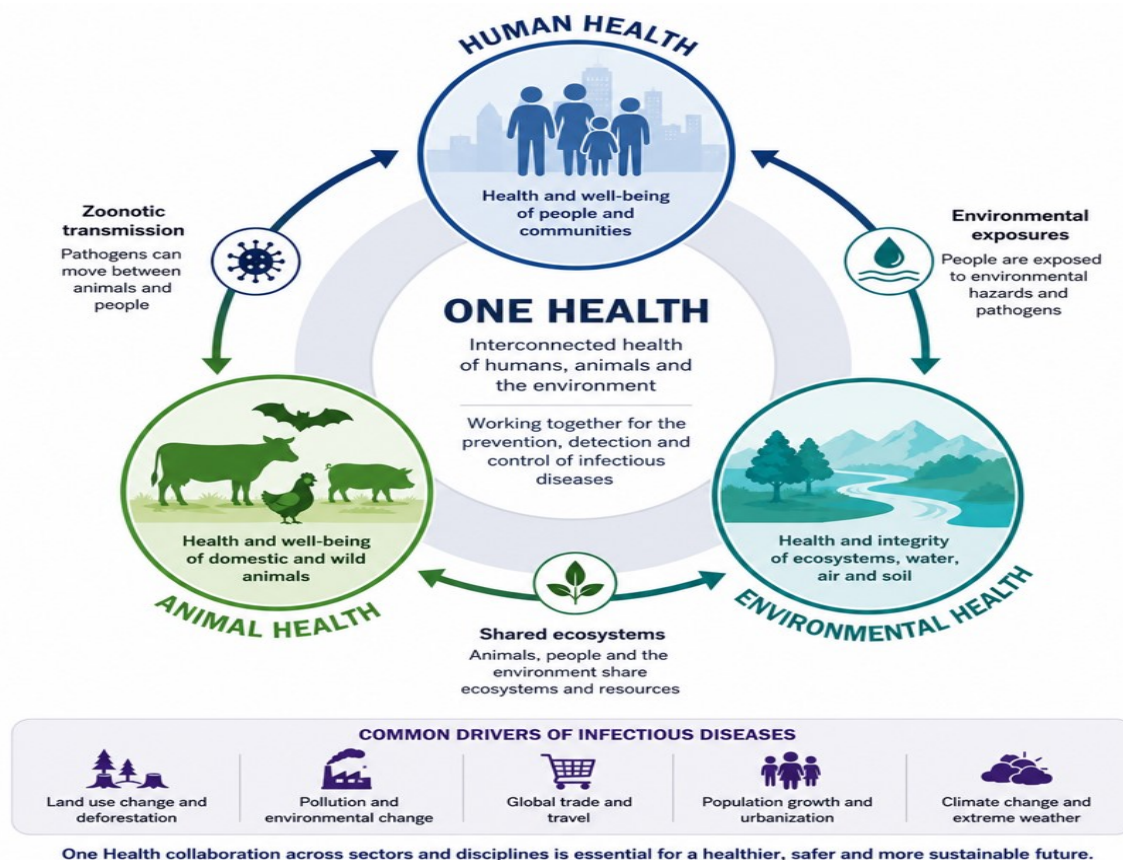
Bacterial infections in diverse geographic and clinical settings further illustrate the epidemiological breadth of the One Health

challenge. Studies of urinary tract infection isolates, dental caries microbiomes, and *Pseudomonas aeruginosa* antibiotic sensitivity patterns across different regions have collectively revealed how microbial communities and their resistance profiles are shaped by local prescribing practices, agricultural antibiotic use, and environmental contamination [39, 40](Table 1). These are not isolated clinical observations. They are signals of larger systemic processes that connect human health to animal husbandry practices, agricultural chemical use, and environmental microbial ecology in ways that demand genuinely integrated responses(Figure 1).

Table 1: Key Infectious Diseases in One Health Context: Transmission Routes, Reservoir Hosts, and Environmental Drivers

Disease/Pathogen	Human Impact	Animal/Environmental Reservoir	Primary Transmission Route	One Health Intervention
Intestinal helminths	Growth retardation, anemia	Soil, animal feces	Feco-oral, soil contact	WASH programs, mass drug administration
Intestinal protozoa (<i>Giardia</i> , <i>Entamoeba</i>)	Diarrhea, malnutrition	Water, animal hosts	Contaminated water	Water treatment, sanitation
Tineacapitis	Scalp infection, alopecia	Soil, animals, fomites	Direct/indirect contact	Environmental hygiene, antifungal treatment
HPV (high-risk types)	Cervical cancer	Human reservoir	Sexual transmission	Vaccination, screening
<i>T. b. rhodesiense</i>	Sleeping sickness, seizures	Cattle, wildlife	Tsetse fly bite	Vector control, reservoir management
<i>Pseudomonas aeruginosa</i>	Respiratory, wound infections	Water, soil, hospital environment	Direct contact, aerosol	Stewardship, environmental control
Oral candidiasis	Oral thrush	Human microbiome, environment	Endogenous, contact	Antifungal therapy, immune support

Figure 1: One Health Triad - Interconnections Between Human, Animal, and Environmental Health in Infectious Disease Epidemiology



3. Antimicrobial Resistance: A One Health Crisis

If there is one issue that exemplifies the One Health principle more vividly than any other, it is antimicrobial resistance. Resistance does not develop separately in human patients, farm animals, and environmental microbes and then accidentally converge. It develops across all these settings simultaneously, driven by shared selection pressures, connected microbial populations, and the movement of resistant organisms and resistance genes through food chains, water systems, and human travel [41, 42]. Understanding resistance through a One Health lens is not just academically interesting. It is practically essential for designing interventions that can actually work [43, 8].

Pseudomonas aeruginosa is a particularly instructive organism in this context. Its natural habitat spans soil, water, plant surfaces, and clinical environments, making it a genuine bridge between environmental and clinical microbiology. Studies examining its antibiotic sensitivity patterns, particularly against fluoroquinolones, have revealed resistance profiles that reflect both clinical prescribing pressures and environmental antibiotic contamination from agricultural runoff and pharmaceutical manufacturing effluents [44, 9]. The organism's extraordinary metabolic versatility allows it to survive and acquire resistance determinants across diverse ecological niches, making it simultaneously an environmental organism and a dangerous nosocomial pathogen.

Staphylococcus aureus and its multidrug resistance mechanisms present a somewhat different but equally complex One Health picture. The MepA multidrug export protein, which actively expels antimicrobial agents from bacterial cells, has been studied through computational approaches that revealed unexpected interactions with non-antibiotic drugs including tramadol hydrochloride [45, 15]. This finding is interesting not only for its repurposing implications but also because it highlights how broadly distributed efflux mechanisms are across bacterial populations and how difficult they are to circumvent with conventional antibiotic strategies alone. Livestock-associated methicillin-resistant *S. aureus* strains have been documented crossing from animal to human populations through direct contact and food handling, underscoring the animal health dimension of staphylococcal resistance [46, 47].

Beta-lactamase producing *Klebsiella pneumoniae* represents one of the most clinically urgent resistance challenges in hospital settings globally. TEM-type beta-lactamases have rendered broad-spectrum penicillins and early cephalosporins largely ineffective against many clinical isolates, and the emergence of carbapenemase-producing strains has further narrowed therapeutic options to the point where some infections have essentially no reliable treatment [48, 49]. Novel peptide-based approaches targeting the beta-lactamase TEM enzyme have been explored through in silico methods, with results suggesting that peptides derived from *Boerhavia diffusa* may interact with the resistance enzyme in ways that could potentially restore antibiotic sensitivity [50, 16]. These are still early-stage findings, but they point toward a creative strategy for addressing one of the most intractable resistance problems in clinical medicine.

Antifungal resistance adds another dimension to this already complex picture. The widespread agricultural use of azole fungicides has created environmental reservoirs of azole-resistant *Aspergillus fumigatus* strains that can cause difficult-to-treat infections in immunocompromised patients who have never received antifungal therapy themselves [51, 52]. This is perhaps the purest expression of the One Health resistance problem, where a patient's treatment failure results directly from agricultural practices occurring in entirely different geographic locations. Studies on oral *Candida* isolates from school children have similarly shown emerging fluconazole resistance patterns that may reflect both clinical and environmental selection pressures operating simultaneously [53, 11].

The environmental reservoir of resistance deserves particular attention within a One Health framework. Antibiotic resistance genes have been detected in soil, water, and air samples from agricultural areas, hospital effluents, and even remote environments far from obvious sources of antibiotic contamination [54, 55](Table 2). This environmental resistome represents a vast and largely unmapped reservoir of genetic material that can be acquired by clinical pathogens through horizontal gene transfer, continuously replenishing resistance capacity in ways that clinical stewardship programs alone cannot address. Effective management of the resistance crisis therefore requires environmental surveillance and remediation strategies that complement clinical prescribing guidelines, a genuinely integrated One Health approach [56, 57].

Table 2: Antimicrobial Resistance in One Health Perspective: Pathogens, Resistance Mechanisms, and Cross-Sector Drivers

Pathogen	Resistance Mechanism	Human Clinical Impact	Animal/Environmental Link	One Health Strategy
<i>Pseudomonas aeruginosa</i>	Efflux pumps, porin loss	Nosocomial infections	Environmental water, soil	Stewardship, environmental monitoring
<i>Staphylococcus aureus</i> (MRSA)	MecA, MepA efflux	Skin, wound, systemic infections	Livestock-associated strains	Cross-sector surveillance
<i>Klebsiella pneumoniae</i>	TEM beta-lactamase, carbapenemase	Hospital-acquired pneumonia, UTI	Food animals, hospital environment	Novel peptides, stewardship
<i>Candida albicans</i>	Azole efflux, target mutation	Oral thrush, systemic candidiasis	Agricultural azole fungicide use	Environmental monitoring
<i>Aspergillus fumigatus</i>	Cyp51A mutation	Invasive aspergillosis	Agricultural triazole exposure	Cross-sector azole stewardship
<i>Escherichia coli</i>	ESBL, plasmid-mediated	UTI, bacteremia	Food animals, water	Integrated surveillance

4. Environmental Biotechnology and Ecological Health

Environmental biotechnology sits at one of the most productive intersections in all of applied science. It brings together microbiology, ecology, chemistry, and engineering to address problems that range from industrial waste treatment to the detection of environmental pathogens to the sustainable production of valuable biochemicals from biological waste streams [59, 60]. Within a One Health framework, environmental biotechnology is not a peripheral concern. It is actually central, because the health of microbial communities in soil, water, and air directly determines the ecological conditions within which human and animal diseases emerge, persist, and spread [61, 17].

The production of valuable biochemicals from biological waste represents one of the more exciting recent developments in environmental biotechnology. Research demonstrating the production of oleic acid from mango kernel waste

using probiotic bacteria isolated from marine fish is a compelling example of how microbial biotechnology can simultaneously address agricultural waste management and generate commercially valuable products [62, 21]. Marine microorganisms have proven to be particularly rich sources of novel enzymatic capabilities, reflecting the evolutionary pressures of deep-sea and coastal environments that have driven the development of metabolic pathways quite different from those found in terrestrial bacteria. This kind of circular bioeconomy approach reduces the environmental burden of agricultural processing waste while creating new value chains that support sustainable development goals.

Nanomaterials have emerged as powerful tools for both environmental remediation and biological applications within the One Health framework. The intersection of nanotechnology and environmental science has generated growing interest in engineered nanoparticles for detecting and removing environmental contaminants including heavy metals, persistent organic

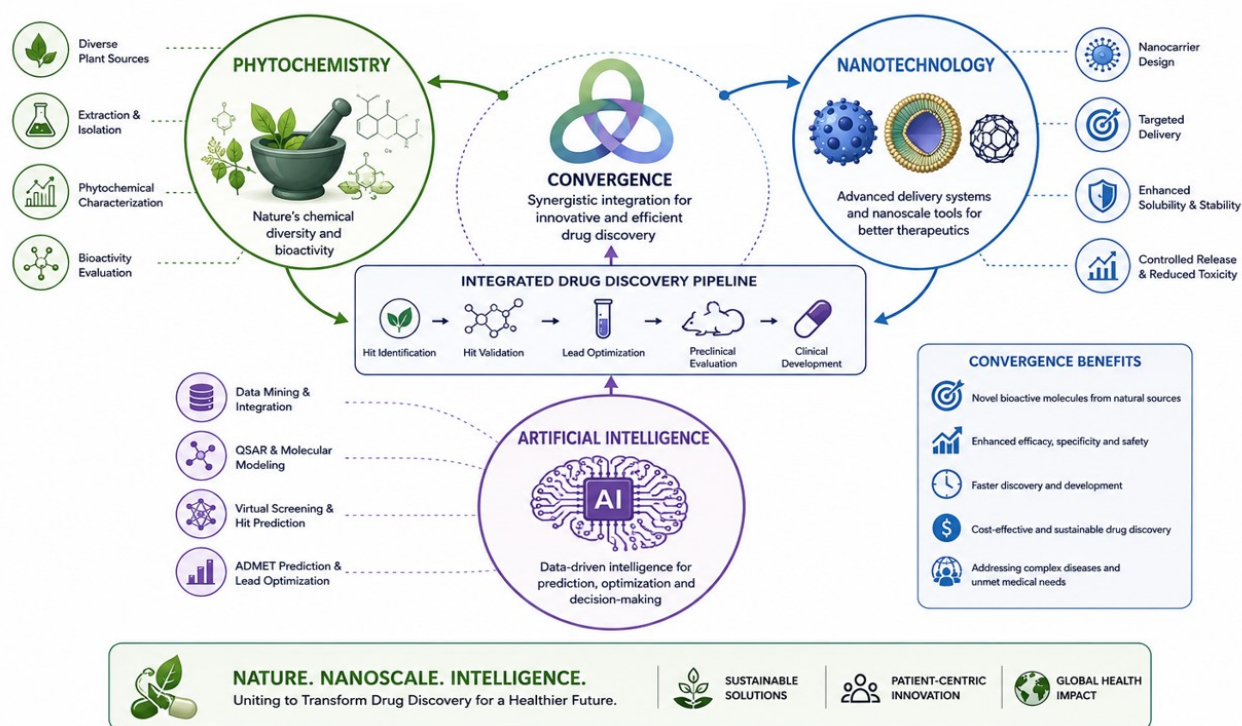
pollutants, and microbial pathogens from water and soil systems [63, 19]. Silver nanoparticles biosynthesized from plant extracts like *Terminalia chebula* have demonstrated potent antimicrobial and antifungal activities that make them interesting candidates for both clinical and environmental applications [64, 20]. The green synthesis approach, where plant phytochemicals serve as both reducing and capping agents, offers a more sustainable and potentially less toxic alternative to chemically synthesized nanoparticles whose environmental fate and ecotoxicological impacts remain incompletely understood.

The environmental dissemination of antimicrobial resistance genes through water systems, agricultural soils, and atmospheric particles represents one of the most pressing ecological health concerns within the One Health framework. Nanomaterial-based sensors capable of detecting resistance genes and resistant organisms at very low concentrations in environmental samples could transform resistance surveillance from a reactive clinical activity into a proactive ecological monitoring system [65, 66]. The editorial contribution highlighting nanomaterials in environmental pollution and sustainable advanced technologies has drawn attention to precisely this kind of application, where nanotechnology serves environmental health goals that ultimately feed back into human and animal health outcomes [45, 67].

Microbial community ecology in agricultural environments has direct implications for human infectious disease risk. The use of antibiotics in

livestock production selects for resistant organisms in animal gut microbiomes that can then be transmitted to humans through food handling, direct animal contact, and environmental contamination of water and produce [68, 69]. Probiotic and prebiotic interventions in animal husbandry represent a One Health biotechnology strategy for reducing antibiotic dependence in livestock production while maintaining animal health outcomes, with potential downstream benefits for human resistance burden [70, 71].

These are not trivial applications. They represent a genuine systemic intervention at the human-animal-environment interface where resistance selection pressures are most intense. Phytoremediation and microbial bioremediation of contaminated environments offer additional tools for reducing the ecological drivers of infectious disease emergence. Heavy metal contamination, pesticide accumulation, and industrial effluent pollution create environmental stresses that destabilize native microbial communities, reduce ecosystem resilience, and create conditions favorable for the proliferation of opportunistic pathogens [72, 73] (Figure 2). Biotechnological strategies for restoring contaminated environments, whether through engineered microorganisms, plant-microbe partnerships, or nanomaterial-assisted remediation, therefore contribute to infectious disease prevention at an ecological level that conventional public health interventions cannot easily reach. This is One Health thinking in its most practical and expansive form.

Figure 2: Environmental Biotechnology Contributions to One Health Outcomes

5. Phytochemical Therapeutics and Natural Product Drug Discovery

Natural product chemistry has a long and genuinely productive history in medicine. A remarkable proportion of the drugs currently in clinical use are either derived from natural sources or inspired by natural product structures, and the pipeline of plant-derived candidates continues to generate leads that synthetic chemistry alone has struggled to replicate [76, 77]. Within a One Health framework, the relevance of phytochemical research extends beyond simple drug discovery. Plants are themselves ecological actors, their chemical diversity shaped by millions of years of co-evolution with pathogens, herbivores, and environmental stressors that parallel the biological challenges facing human and animal health [78, 79].

Boerhaavia diffusa has established itself as one of the most consistently interesting medicinal plants in contemporary natural product research. Phytochemical screening has revealed a rich

profile of alkaloids, flavonoids, phenolic compounds, and rotenoids, and biological evaluations have demonstrated meaningful antioxidant, anti-inflammatory, antibacterial, and anticancer activities across multiple experimental models [80, 81]. Cytotoxic studies against human cancer cell lines have shown dose-dependent inhibitory effects that point toward apoptosis induction as a likely mechanism, and in silico peptide design studies using protein sequences derived from this plant have opened up entirely new avenues for computational drug development [82, 12]. The consistency of findings across different research groups and experimental systems adds genuine credibility to the case for advancing *B. diffusa* into more systematic preclinical investigation.

Euphorbia hirta presents a comparably interesting profile. Preliminary phytochemical screening has confirmed the presence of flavonoids, saponins, tannins, and phenolic acids, and antibacterial assays have demonstrated activity against clinically relevant organisms [83, 84]. More sophisticated analyses using GC-MS and FT-IR

metabolite profiling have allowed researchers to characterize the chemical complexity of *E. hirta* extracts with greater precision, while cytotoxic evaluation against SiHa cervical cancer cells has revealed antiproliferative effects that warrant further mechanistic investigation [85, 86]. What makes *E. hirta* particularly interesting from a One Health perspective is its traditional use across multiple cultures for treating both infectious and inflammatory conditions in humans and animals, suggesting an evolutionary context for its broad biological activity.

Tephrosia purpurea extracts have demonstrated meaningful antibacterial activity against tomato spoilage pathogens, which is interesting for several reasons beyond the obvious agricultural application [87, 88]. Food spoilage pathogens represent a genuine One Health concern, sitting at the interface of plant health, food safety, and human infectious disease risk. The antibacterial activity of *T. purpurea* against these organisms suggests potential applications in sustainable agricultural pest management that could reduce reliance on synthetic fungicides and bactericides whose environmental residues contribute to the ecological resistance burden [89, 60]. This is a small but instructive example of how phytochemical research can generate insights with simultaneous relevance across plant, human, and environmental health domains.

Achyranthes aspera and *Ficus carica* have both demonstrated promising anticancer profiles in laboratory settings. Methanolic extracts of *A. aspera* have shown antioxidant activity and cytotoxicity against SiHa cervical cancer cells, while *F. carica* extracts evaluated against MCF-7 breast cancer cells have demonstrated growth inhibition consistent with phenolic and flavonoid-mediated antiproliferative effects [90, 91]. *Ipomoea obscura*, assessed for antioxidant, anti-inflammatory, antibacterial, and anticancer activities, has shown a broad-spectrum biological profile that is characteristic of complex plant extracts containing multiple synergistically acting constituents [92, 93]. These findings collectively reinforce the value of systematic phytochemical

investigation as a productive strategy for identifying new therapeutic leads.

The methodological evolution in phytochemical research deserves acknowledgment within this discussion. The field has moved steadily from simple extract-based bioassays toward more sophisticated approaches involving cell-based cytotoxicity models, advanced spectroscopic characterization, and increasingly, computational methods for predicting how plant-derived compounds interact with specific molecular targets [94, 95]. Silver nanoparticles biosynthesized from *Terminalia chebula* extracts represent an interesting hybrid approach that combines nanotechnology with phytochemistry, where plant compounds serve simultaneously as synthesis agents and biological activity enhancers [96, 64].

6. Computational Drug Discovery and Therapeutic Innovation

Computational approaches have quietly transformed the early stages of drug discovery in ways that are still not fully appreciated outside specialist circles. The ability to model molecular interactions between candidate compounds and target proteins, to predict pharmacokinetic properties before any laboratory work begins, and to design entirely novel peptide sequences optimized for specific binding geometries has compressed the front end of the drug discovery pipeline in ways that were genuinely unimaginable two decades ago [97, 98]. Within a One Health framework, these capabilities are particularly valuable because they allow researchers to address multiple disease targets across human, animal, and vector biology using shared computational infrastructure and methodological expertise.

Molecular docking has become the workhorse of computational drug discovery, and its application across infectious disease and cancer targets has generated a steady stream of promising candidates for experimental validation. Studies designing novel peptides targeting *Anopheles gambiae*

proteins have demonstrated how in silico approaches can accelerate vector-control drug discovery, identifying selective candidates that would have required years of conventional screening to find through experimental methods alone [99, 100]. Similarly, computational protocols applied to *Culex quinquefasciatus* proteins have yielded de novo peptide candidates with favorable binding profiles that support progression to experimental validation [51, 53]. These mosquito-targeted studies are directly relevant to One Health because vector control sits precisely at the interface of human health, ecological systems, and environmental management.

Drug repurposing through computational screening has emerged as one of the most pragmatically attractive strategies in modern therapeutics. The computational evaluation of linezolid and ciprofloxacin against mutant ESR1 protein in breast cancer illustrates how antibiotics developed for infectious disease indications may harbor previously unrecognized anticancer potential that would never have been discovered without systematic in silico investigation [39, 57]. This kind of cross-indication discovery resonates strongly with One Health thinking, because it reflects the same integrative logic of looking beyond conventional disciplinary boundaries to find solutions that transcend the categories we impose on biology. The biology of cancer cells and the biology of bacterial pathogens are obviously different, but the computational tools for probing protein-ligand interactions work across both domains with equal facility.

Peptide-based drug design represents perhaps the most exciting frontier in computational therapeutics within a One Health context. Peptides can be designed with extraordinary specificity for particular protein targets, and the diversity of biological systems accessible to peptide-based intervention is enormous. The 3D peptide-protein docking study examining interactions between a novel peptide derived from *Boerhavia diffusa* and the cervical cancer protein transmembrane protein 50A has demonstrated how plant-derived molecular information can be

computationally translated into targeted anticancer candidates [31, 82]. Peptide-based medicines designed against *Aedes aegypti* proteins extend this approach into vector biology, offering possibilities for highly selective vector-control agents that minimize ecological collateral damage compared to broad-spectrum insecticides [49, 85].

The computational evaluation of tramadol hydrochloride against the MepA efflux protein of *Staphylococcus aureus* represents a particularly creative application of drug repurposing methodology [27, 45]. Anti-inflammatory drugs are not intuitively obvious candidates for antibacterial repurposing, but the computational evidence suggesting that tramadol may interact with and inhibit the MepA efflux pump opens up an entirely new way of thinking about how existing pharmacological agents might be deployed against resistant organisms. This kind of unexpected cross-domain insight is one of the most valuable products of systematic computational screening, and it exemplifies the lateral thinking that One Health perspectives both require and reward.

The future of computational drug discovery within One Health is closely tied to advances in artificial intelligence and structural biology. AlphaFold's remarkable success in predicting protein structures from amino acid sequences alone has dramatically expanded the universe of tractable drug targets, including proteins from neglected tropical disease pathogens and vector organisms for which experimental structural data was previously unavailable [58, 97]. Machine learning approaches are increasingly being applied to predict antimicrobial activity, toxicity, and pharmacokinetic properties of candidate molecules, further accelerating the pipeline from computational hit identification to experimental validation. These developments are democratizing drug discovery in ways that align naturally with One Health priorities, enabling researchers in lower-resource settings to contribute meaningfully to global therapeutic innovation.

7. Vector-Borne Diseases and Integrated Control Strategies

Vector-borne diseases occupy a unique position within the One Health framework because they inherently require simultaneous attention to human hosts, animal reservoirs, insect vectors, and the environmental conditions that support vector populations. Malaria, dengue, filariasis, trypanosomiasis, and a growing list of emerging arboviral infections collectively affect billions of people globally, with their geographic distribution shaped by ecological factors including temperature, rainfall, land use change, and biodiversity loss that connect human health directly to planetary health [58, 100]. Managing these diseases effectively is impossible without engaging all three domains of the One Health triad.

Mosquito-borne diseases represent the largest single category of vector-borne disease burden globally. *Anopheles gambiae* is the primary vector of *Plasmodium falciparum* malaria in sub-Saharan Africa, where the disease continues to cause hundreds of thousands of deaths annually despite decades of intensive control efforts. Novel peptide-based approaches targeting *A. gambiae* proteins identified through in silico screening represent an innovative contribution to vector control research, offering the possibility of highly specific interventions that could complement existing tools like insecticide-treated bed nets and indoor residual spraying [23, 99]. The development of resistance to pyrethroids and other insecticide classes in *Anopheles* populations has made the search for alternative vector control strategies genuinely urgent, and computational peptide design is one of the more creative responses to this challenge.

Culex quinquefasciatus is the primary vector of lymphatic filariasis and several arboviral diseases across tropical and subtropical regions. De novo peptide candidates designed through computational protocols targeting *C. quinquefasciatus* proteins represent an interesting parallel to the *Anopheles*-directed research,

suggesting that in silico vector-control drug discovery may be applicable across multiple mosquito species with relatively modest additional investment [80-83]. *Aedes aegypti*, the vector of dengue, Zika, chikungunya, and yellow fever, has similarly been targeted through peptide-based in silico approaches, with candidate molecules showing favorable computational profiles that support further experimental evaluation [84-88]. Taken together, these studies suggest that computational peptide design is emerging as a genuinely productive platform for vector-control drug discovery across multiple disease-relevant species.

Human African trypanosomiasis caused by *Trypanosoma bruceirhodesiense* illustrates the animal reservoir dimension of vector-borne One Health challenges with particular clarity. Cattle and wildlife serve as reservoir hosts for rhodesiense trypanosomes, and the tsetse fly vectors that transmit the parasite to humans are intimately associated with savanna ecosystems whose integrity is threatened by land use change and habitat fragmentation. Studies examining seizure prevalence in stage-two rhodesiense trypanosomiasis have highlighted the severe neurological consequences of late-stage infection and the clinical management challenges posed by central nervous system involvement in resource-limited settings [89-91]. Addressing this disease requires coordinated intervention across human medicine, veterinary medicine, vector control, and ecosystem management, making it perhaps the most complete expression of One Health complexity in the parasitology literature.

The environmental determinants of vector-borne disease distribution are increasingly well understood and increasingly alarming. Climate change is expanding the geographic range of several major vector species, bringing malaria, dengue, and other diseases into regions previously considered non-endemic [92-95]. Deforestation and agricultural expansion are creating edge habitats that favor certain vector species while disrupting the ecological checks that normally limit their populations. Urbanization is generating ideal breeding environments for *Aedes*

mosquitoes in the form of water storage containers, discarded tires, and blocked drainage systems. These ecological drivers of disease emergence are fundamentally One Health problems that require environmental management solutions alongside medical and veterinary interventions [95, 96].

Integrated vector management, which combines biological control, environmental management, chemical control, and community engagement within a unified strategic framework, represents the most coherent One Health response to the vector-borne disease challenge. Biological control agents including predatory copepods, larvivorous fish, and entomopathogenic bacteria offer environmentally sustainable alternatives to chemical insecticides that are fully consistent with One Health principles of minimizing ecological collateral damage [97]. Community engagement and environmental education are essential components of any sustainable vector control program, because many of the most effective interventions, eliminating breeding sites, using bed nets, maintaining drainage systems, require sustained behavioral changes at the community level that no top-down intervention can achieve alone.

8. Oral Health, Disability, and Microbiome Perspectives

Oral health occupies an interesting and somewhat underappreciated position within the One Health framework. The oral microbiome is one of the most complex and dynamic microbial communities in the human body, and its composition reflects influences ranging from diet and hygiene to systemic immune status, antibiotic exposure, and environmental microbial ecology [98-100]. Disruptions to oral microbial balance are associated not only with dental caries and periodontal disease but with systemic conditions including cardiovascular disease, diabetes, and adverse pregnancy outcomes, making oral health a window into broader systemic and ecological health.

Studies on the microbiology of dental caries have revealed a complex community of organisms including *Streptococcus mutans*, lactobacilli, and various anaerobes that interact dynamically within the oral biofilm environment [101-104]. The isolation and characterization of caries-associated microbes from community settings have provided valuable insights into the microbial ecology of this extremely common disease, whose prevalence across populations reflects dietary patterns, fluoride exposure, oral hygiene practices, and access to dental care in ways that connect individual health to social and environmental determinants [105-107]. Understanding the microbiological basis of dental caries more deeply has direct implications for the development of targeted antimicrobial and probiotic strategies for prevention and treatment.

Oral health challenges in populations with mental, physical, and social disabilities represent a particularly important and often neglected dimension of the microbiome story. Studies examining oral microbial diseases in people with disabilities have highlighted how physical limitations, cognitive impairments, and social isolation combine to create conditions of poor oral hygiene and elevated infection risk that conventional dental care systems are poorly equipped to address [108]. The microbial consequences of these vulnerabilities, including elevated rates of oral candidiasis, dental caries, and periodontal disease, reflect systemic inequities in health access that have both individual and population-level consequences. Addressing oral health in these populations requires not just better clinical protocols but genuinely inclusive health system design that reaches people whose needs fall outside conventional service delivery models.

Urinary tract infections in diverse geographic settings offer another perspective on how environmental and systemic factors shape microbial disease patterns. Studies of bacterial isolates from urinary tract infections across different regions have revealed patterns of mixed flora with varying antibiotic sensitivity profiles that reflect local prescribing practices and

environmental resistance reservoirs [109-111]. The geographic variability of these patterns is itself informative, suggesting that resistance profiles in clinical settings are shaped by community-level antibiotic use and environmental contamination as much as by hospital prescribing practices. This is a One Health observation with direct practical implications for empirical treatment guidelines, which need to be locally calibrated rather than universally applied.

The intersection of viral infections and systemic vulnerability brings the discussion back to HPV and HIV co-infection, which represents one of the clearest examples of how immunological compromise amplifies infectious disease risk across multiple pathogen categories simultaneously. Studies consistently showing elevated rates of HPV-16 and other high-risk HPV types among HIV-positive women have important implications for cervical cancer screening and prevention programs in high-burden settings [112]. The immunological mechanism is straightforward, impaired cell-mediated immunity allows HPV to persist and progress toward oncogenic transformation more readily than in immunocompetent hosts, but the clinical and public health implications are complex, requiring integrated HIV and cervical cancer management programs that neither HIV nor oncology services alone are typically designed to provide.

9. Aging, Chronic Disease, and One Health Intersections

The relationship between aging, chronic disease, and infectious disease risk is one of the most clinically important and least adequately addressed dimensions of the One Health framework. Older adults face elevated risks from virtually every category of infectious disease discussed in this review, partly because of age-related immune senescence and partly because of the accumulated physiological vulnerabilities that make clinical management of infections more complex and outcomes less predictable [113-115].

Understanding these vulnerabilities in their full physiological and social context is essential for designing healthcare interventions that actually serve aging populations effectively.

Orthostatic hypotension is a common but often under recognized condition in older adults that has significant implications for both physical and mental health outcomes. Studies examining the impact of aging on orthostatic hypotension have highlighted how this cardiovascular vulnerability interacts with other aspects of physiological decline to increase fall risk, cognitive impairment, and overall functional deterioration in ways that complicate both infectious disease management and broader chronic disease care [116, 117]. In a One Health context, the mental health dimensions of aging are particularly important because psychological wellbeing influences immune function, treatment adherence, and health-seeking behavior in ways that feed back into infectious disease susceptibility and outcomes.

The pharmacological management of infections in older adults is complicated by polypharmacy, reduced renal and hepatic function, and altered drug distribution that collectively affect both the efficacy and toxicity of antimicrobial agents [118]. Drug repurposing research, including computational studies evaluating existing approved drugs against new microbial and cancer targets, has particular relevance for aging populations because it can potentially identify therapeutic candidates with better safety profiles for older adults than existing first-line agents [119]. The computational evaluation of established drugs like linezolid and ciprofloxacin against cancer targets, and tramadol against bacterial resistance proteins, represents exactly this kind of repurposing thinking that aging medicine increasingly needs.

Chronic infectious diseases, including persistent viral infections like HPV and parasitic infections that may remain subclinical for years, interact with the aging process in complex ways that are not yet fully understood. The immunological changes of aging, including reduced T cell diversity, impaired innate immune responses, and

chronic low-grade inflammation, create conditions that favor reactivation of latent infections and impair clearance of persistent pathogens [120]. These dynamics have direct implications for cancer risk in older adults, where HPV-driven cervical and oropharyngeal cancers, for instance, may emerge decades after initial infection as immune control gradually deteriorates. Understanding these long-term infection-aging interactions is an important frontier for One Health research.

10. Conclusion and Future Perspectives

The One Health framework, when applied honestly and rigorously to the evidence reviewed here, reveals something both sobering and genuinely encouraging. The sobering part is the sheer complexity and interconnectedness of the challenges, where resistant pathogens, environmental contamination, vector ecology, aging populations, and therapeutic gaps all feed into each other in ways that resist simple solutions. The encouraging part is that the scientific tools, computational biology, phytochemical research, nanotechnology, environmental biotechnology, and integrated surveillance, are becoming increasingly sophisticated and increasingly connected to each other in exactly the ways that One Health demands.

The epidemiological evidence reviewed across sections makes clear that infectious diseases continue to impose enormous burdens on human and animal populations, particularly in resource-limited settings where environmental and social determinants of health remain inadequately addressed. Addressing these burdens requires not only better drugs and diagnostics but stronger health systems capable of implementing integrated interventions across human, animal, and environmental health domains simultaneously. This is a governance and political challenge as much as a scientific one, and scientific innovation alone cannot substitute for

the sustained institutional commitment that genuine One Health implementation requires.

Phytochemical research has matured into a credible contributor to the therapeutic pipeline, with plants like *Boerhaavia diffusa*, *Euphorbia hirta*, *Achyranthes aspera*, and *Ficus carica* generating laboratory evidence that justifies continued systematic investigation. The challenge now is bridging the gap between promising in vitro findings and validated in vivo efficacy through systematic preclinical development, toxicological profiling, and ultimately clinical evaluation. This requires investment, patience, and the kind of methodological rigor that moves natural product research from interesting observation to genuine therapeutic contribution.

Computational drug discovery has demonstrated its value as both an accelerator and a democratizer of therapeutic innovation. In silico approaches have identified novel peptide candidates against multiple disease targets, revealed repurposing possibilities for existing drugs, and generated mechanistic insights into resistance biology that experimental approaches alone would have struggled to produce. As artificial intelligence and structural prediction tools continue to advance, their integration into One Health drug discovery programs will create increasingly powerful capabilities for addressing the full spectrum of human, animal, and vector disease targets within unified research frameworks.

Environmental biotechnology and nanotechnology are contributing tools for both disease management and ecological health restoration that sit naturally within One Health priorities. Green synthesis of bioactive nanoparticles, microbial waste valorization, environmental resistance surveillance, and probiotic-based livestock management all represent practical expressions of One Health biotechnology that deserve continued investment and regulatory attention. The safety assessment of nanotechnology-based interventions remains an important parallel priority, ensuring that therapeutic innovation does not inadvertently create new ecological risks.

Ultimately, the One Health perspective reviewed here points toward a future in which the boundaries between human medicine, veterinary science, environmental health, and ecological science become progressively less relevant than the connections between them. The diseases, the pathogens, the resistance mechanisms, and the therapeutic solutions all flow across these boundaries with complete indifference to the disciplinary categories we have constructed around them. Meeting them effectively requires that our science, our institutions, and our thinking do the same.

Conflict of interest

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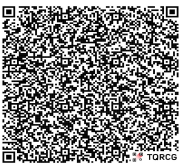
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