Natural Compounds From Vietnamese Medicinal Herbs At The Intersection Of Cancer Cell Proliferation And Cellular Ageing: An Integrative Review Of Experimental Evidence And Ecological Determinants

Khoa Dang Dang
Lac Hong University, Department of Biological Sciences

Abstract:

Cancer continues to represent one of the leading causes of mortality worldwide, accounting for millions of deaths each year and placing immense economic and social strain on healthcare systems. According to WHO (2025), Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths. Furthermore, Ageing is a biological process that is based on the loss of cellular functionality and is intertwined with the development of cancer to an extent. Moreover, senescence refers to the permanent growth arrest of cells that develops with age and involves profound molecular and metabolic alterations. Consequently, according to Alavimanesh et al. (2025) senescent cells release proinflammatory cytokines, growth factors, and proteases collectively known as the senescence associated secretory phenotype, which alter the tissue microenvironment and, under specific conditions, facilitate tumour initiation. Simultaneously, the process of senescence has the potential to inhibit the malignant transformation by preventing the proliferation of the damaged cells. This bivalent property of ageing and senescence has generated a scientific interest in compounds that have the ability to regulate these pathways to inhibit cancer progression or slow down cellular decay. Natural products of medicinal herbs have offered some of the most promising therapeutic leads in oncology and gerontology over the past decades. In addition, according to Tungmunnithum et al. (2018) Plant molecules like alkaloids, flavonoids, terpenoids, and phenolic acids have a variety of biological effects, including induction of apoptosis, inhibition of oxidative stress and inflammation. Their structural diversity, ecological adaptation and biochemical specificity make them valuable templates of drug discovery.

INTRODUCTION

Vietnam is the country where these relationships can be studied in a unique way because of its outstanding biodiversity and a long-standing culture and ecological diversity-based herbal medicine tradition (Nguyen 2024). Tropical climate, the diversity of the topography, and ecosystems of the country support thousands of medicinal species of plants, most of which are endemic or adapted to the region. According to Ekiert et al. (2021) Traditional Vietnamese pharmacopoeia has employed genera such as *Croton*, *Garcinia*, and *Artemisia* for centuries to treat ailments including inflammation, tumours, and age-related conditions. These applications are starting to be supported by modern phytochemical and pharmacological research which has identified bioactive compounds- ent-kaurane diterpenoids, xanthones, flavonoids and sesquiterpenes- which display cytotoxic, antioxidant, and anti-senescence activity (Traore et al. 2023). Studies like Kamau et al. (2025) and Andreani et al. (2024) reported in local and global journals including J-STAGE and Springer Nature Experiments have reported several novel compounds with selective antiprolliferative actions against cancer cell lines, but have not been synthesised systematically to report on their mechanistic role and ecological origin. The overlap between cancer cell proliferation and cellular ageing creates a conceptual base of fertile integration inquiry due to the similarity in molecular networks of p53/p21, telomerase, NF-kB, mTOR, and reactive oxygen species (ROS) regulation mediating tumour suppression and ageing alike (Roake and Artandi 2017). These convergent pathways are frequently regulated by botanical compounds, implying that their impact on cancer and senescence are not independent phenomena but mechanistically linked. Although it has shown encouraging results, the research on Vietnamese medicinal herbs is still scattered and little studies have been combined to assess anticancer and anti-ageing effects, as well as to test ecological factors like plant habitat, extraction methods, and the traditional ethnobotanical settings that can affect bioactivity.

The current review examines experimental evidence on bioactive compounds derived from Vietnamese medicinal herbs and their effects on cancer cell proliferation and cellular ageing. It further evaluates how ecological diversity and ethnobotanical knowledge influence these biological activities, integrating molecular, environmental, and cultural perspectives within a single analytical framework.

METHODOLOGY

The review adopted an integrative review design because it allowed the synthesis of experimental, ecological, and ethnobotanical evidence within a single analytical framework. In contrast to a systematic or narrative review, the integrative approach encompassed both quantitative and qualitative data of heterogeneous origin and made it possible to obtain a comprehensive perspective regarding the effect of Vietnamese herbal compounds on the proliferation and the ageing of cancer cells. This approach was chosen, rather than a meta-analysis or Systematic Literature Review, because the available studies differed in design, endpoints, and metrics of reporting, which did not allow statistical pooling (Ahn and Kang 2018). The method used adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) framework to make the literature selection, screening, and synthesis transparent.

The PICO Framework

To organise the review question and evidence extraction, the PICO framework (Population, Intervention, Comparison, and Outcome) was selected. PICO was chosen over PEO (Population, Exposure, Outcome) since the studies to be reviewed included active experimental interventions-testing of natural compounds of Vietnamese medicinal herbs on cancer and ageing models-as opposed to passive exposure to conditions. Schiavenato and Chu (2021) argue that PICO is better clarified and reproducible in biomedical research where intervention-based research prevails, and precise mapping of biological effects and outcomes is achievable. The framework was a structured synthesis because it aligned experimental evidence on herbal compounds (Intervention) with the quantifiable biological responses on proliferation inhibition, oxidative stress reduction, and senescence modulation (Hosseini et al. 2024). Application of PICO improved methodological rigour and consistency across diverse experimental designs and allowed comparison of trends of bioactivity across studies. The following table demonstrates the identified PICO elements used in the review.

Table 1: PICO Framework

Element	Description
Population (P)	Experimental models involving cancer cells or ageing-related cellular systems from studies using Vietnamese medicinal herbs
Intervention (I)	Natural compounds or extracts derived from Vietnamese medicinal plants tested for anticancer or anti-ageing effects
Comparison (C)	Control groups or untreated cell lines used to evaluate differences in proliferation and senescence responses
Outcome (O)	Measured effects on cancer cell proliferation, apoptosis, oxidative stress, telomere dynamics, or cellular senescence markers

Search Strategy

The search strategy was formulated to obtain the broadest and most validated evidence on natural compounds found in Vietnamese medicinal herbs and their effects on cancer cell proliferation and cellular ageing. Online databases like PubMed/Medline, Scopus, Web of Science, and repositories of Vietnamese science on the region were intensively searched to cover both global and local content. The literature search covered literature published from 2015-2025 and contained English and Vietnamese studies where a reliable translation could be found. The key concepts were combined logically using Boolean operators and search precision improved-a method upheld by MacFarlane, Russell-Rose and Shokraneh (2022), who advised that Boolean logic increases search accuracy in integrative review by connecting interchangeable concepts and excluding irrelevant information. The Boolean operator aided in combining synonyms (Vietnam OR Vietnamese) with cross-disciplinary variables (anticancer AND senescence) to allow the incorporation of

various terminologies that are employed in both biomedical and ethnopharmacological sources. Seminal review and reference list citation tracking, which was conducted manually, further increased the number of eligible studies. The table below illustrates the Boolean operators and examples of search terms used in the review.

Table 2: Boolean Operators

Boolean Operator	Search Term Example
OR	"Vietnam" OR "Vietnamese"
AND	"medicinal plant" AND "natural compound" AND "cancer cell proliferation" AND "cellular ageing"
AND/OR combined	("Vietnam" OR "Vietnamese") AND ("herb" OR "phytochemical") AND ("anticancer" OR "senescence")

Selection Criteria

The inclusion criteria were focused on primary experimental studies in peer-reviewed English journals available in major scientific databases. Studies that used laboratory-based experimental designs were only included in order to achieve methodological consistency and measurable results. Research employing laboratory-based experimental designs published between 2015 and 2025 were included to ensure methodological consistency, measurable outcomes, and the incorporation of the most recent experimental evidence in the field. The eligible studies were required to involve natural compounds extracted out of Vietnamese medicinal herbs in cancer cell proliferation or models of cellular ageing using in-vitro or in-vivo platforms. All studies had to present either quantitative or qualitative evidence of mechanistic effects including, but not limited to, apoptosis induction, oxidative stress regulation, telomere modulation, or senescence biomarkers. Review papers, meta-analyses, conference abstracts, and studies that were not experimentally validated were omitted. Inclusion of primary studies provided direct empirically linking phytochemical compounds with biological outcomes, as was advised by Dhollande et al. (2021), who emphasised that integrative reviews would become scientifically credible upon synthesis of original data. Such primary experiments were peer-reviewed only to preserve the depth of analysis and its accuracy.

Data Collection and Analysis

Only primary experimental studies were used to extract data because of the empirical reliability and scientific validity in the measurement of biological effects of natural compounds of medicinal herbs used in Vietnam on cancer cell proliferation and cellular ageing. Quantitative measures including the IC50 values, apoptosis percentage, oxidative stress levels, and telomere activity were documented and the qualitative descriptors like classes of compound, mode of extraction, and cellular reaction. Primary studies only were included since, as Varga (2022) confirms, secondary literature tends to dilute the precision of experimental results, when contrasted with direct data, which make it possible to make stronger causal inferences and valid mechanistic synthesis. Thematic analysis was used in the analysis, a method that facilitated the systematic description of common molecular pathways and ecological factors in various datasets. Such a method was preferred to meta-analysis or statistical pooling because of the heterogeneity of designs and measurement units. Ahmed et al. (2025) argue that thematic analysis provides conceptual richness and consistency in combining mixed data types. The approach classified results into mechanistic themes, including apoptosis, cell cycle regulation, oxidative modulation, and senescence control, enabling interpretive depth and contextual understanding.

RESULTS

The initial database search in PubMed, Scopus, Web of Science, and Google Scholar to identify publications included studies that were published between January 2015 and October 2025, resulting in 628 publications. The titles and abstracts of 503 articles were screened after eliminating duplicates and ineligible records. Among these, 475 were eliminated as review papers, conference papers, non-peer-reviewed articles, non-experimental studies, or not related to Vietnamese medicinal herbs. The remaining 28 articles were retrieved to be examined in full text. After the eligibility assessment, 23 articles underwent elimination due to age (more than 2015), lack of relevance to the research objectives, and unavailability or non-Englishness of the

full text. Therefore, there were five major experimental studies that satisfied all inclusion criteria. These chosen studies utilised the laboratory based experimental designs that tested independent variables including phytochemical composition, extraction technique, and compound concentration, and dependent variables including cytotoxicity, induction of apoptosis, regulation of oxidative stress, and modulation of senescence as shown in Figure 1.

Figure 1: Prisma Flowchart
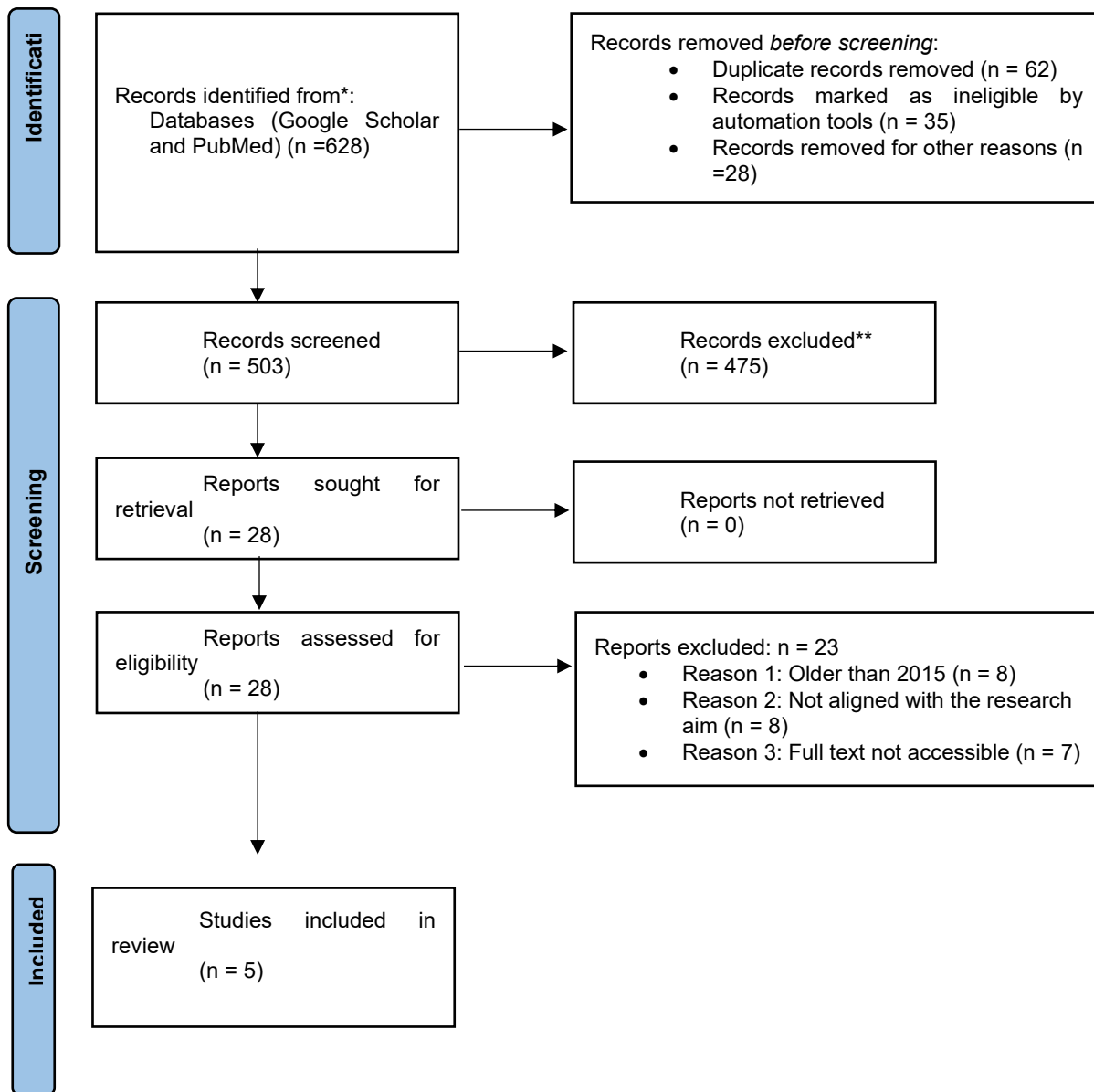
Theme 1 – Mechanistic Pathways Linking Cancer Cell Proliferation and Cellular Ageing

This theme explores the mechanistic pathways through which natural compounds influence both cancer cell proliferation and cellular ageing, revealing overlapping biological targets and molecular processes. The article by Tallei et al. (2025) has presented rosemary as a paradigm herb to demonstrate the dual anti-ageing and anticancer actions using network pharmacology and molecular docking. The study detected flavonoids including cynaroside, myricetin, and kaempferol using LC-HRMS and GC-MS and reacted with regulatory proteins, including p53, AKT1, and SRC. These substances inhibited melanoma growth by 74.7 percent and repressed tyrosinase activity and displayed antioxidative and apoptotic synergy. The key strength of this work was the combination of in vitro experiments with computational validation which provides molecular specificity, but the constraint was that only one model of cancer was studied, and can be generalised. On the

same note, Kim et al. (2020) studied *Peltophorum pterocarpum* through ethanolic extraction and cytotoxic and oxidative stress testing. This experiment proved the activation caspase-3/9 and cleavage of PARP in leukaemia cells, which supported the apoptosis as the key anticancer effect. It was strong in experimental clarity, but depended on crude extracts, and this, in reproducibility and precise compound identification, was disadvantageous.

In contrast, Nguyen et al. (2021) adopted a bioassay-guided fractionation method to isolate potent cytotoxic fractions from *Hyptis suaveolens*, *Luvunga scandens*, and *Solanum torvum*, tested on hepatocellular carcinoma cells. The study demonstrated that ethyl acetate and 90% methanol extracts with high flavonoid content exhibited superior cytotoxicity ($IC_{50} \approx 100$–200 µg/mL), establishing a quantitative link between antioxidant capacity and proliferation inhibition. The approach was systematic and reproducible but constrained by a lack of molecular pathway validation. In comparison, Duong et al. (2023) used bioactive-guided isolation and molecular docking to research *Dicranopteris linearis* and *Psychotria adenophylla*, discovered twenty compounds that possess alpha-glucosidase inhibition and ROS-suppressing properties. This mechanistic overlap facilitated the regulation of oxidative stress as a similar pathway by ageing and cancer. Although it was developed based on advanced compound identification, its weakness was the absence of in vivo testing. All four studies together have shown that the Vietnamese medicinal herbs have convergent molecular mechanisms-oxidative modulation, apoptosis activation, and mitochondrial protection as the bridge mechanism between anti-cancer and anti-ageing potential.

Theme 2 – Phytochemical Diversity and Experimental Evidence of Bioactivity

This theme focuses on the phytochemical diversity and experimental evidence of bioactivity within Vietnamese medicinal herbs and comparable botanical compounds. Nguyen et al. (2021) screened 52 methanol extracts of 24 traditional herbs on hepatocellular carcinoma cells through bioassay-guided fractionation. The article by Nguyen et al. (2021) utilised bioassay-guided fractionation of 24 Vietnamese medicinal plants, where phytochemical diversity was the priority, instead of cytotoxic activity. The extracts showed that the plants with high content of flavonoids and phenolic compounds exhibited higher bioactivity, which emphasises the chemical nature of therapeutic capacity. Such a association between the class of compounds and biological activity highlighted the versatility of the Vietnamese flora with respect to metabolism. This study was also strong because it systematically quantified the antioxidant capacity, and therefore developed a strong correlation between richness of compounds and bioactivity; but its weakness was that it did not provide confirmation of the underlying mechanism of action by molecular-level quantification or pathway-specific validation. Kim et al. (2020) examined Peltophorum pterocarpum through ethanolic extraction, cytotoxic, and oxidative stress test, indicating flavonoids, tannins and phenolics as the major bioactives. Its strength was symptomatic of apoptosis with the manifestation of caspase activation, and the use of crude extracts limited the reproducibility of compounds.

Likewise, Tallei et al. (2025) have used LC-HRMS and GC-MS as well as network pharmacology to map the metabolome of rosemary and identified flavonoids such as cynaroside and kaempferol active against p53, AKT1, and SRC. This complicated method provided structural and mechanistic particularity, even though its single-cell-line focus limited comparative scope. Duong et al. (2023), conversely, undertook bioactive-guided isolation and molecular docking on *Dicranopteris linearis* and *Psychotria adenophylla*, isolating twenty compounds with robust a-glucosidase activity and ROS scavenging, relating metabolic regulation to ageing control. It was strong in terms of compound resolution, but lacked in-vivo testing which limited translational relevance. Collectively, these pieces of evidence suggest that Vietnamese and regional herbs harbour chemically diverse phytochemicals-flavonoids, terpenoids and triterpenes- which display reproducible antioxidant and cytotoxic signatures but necessitate combined analytical and biological validation to support their pharmacological potential.

Theme 3 – Ecological and Ethnobotanical Determinants of Therapeutic Potential

This theme analyses the ecological and ethnobotanical determinants influencing the therapeutic potential of Vietnamese medicinal herbs, illustrating how biodiversity and traditional practices underpin pharmacological discovery. Muhajirin (2024) utilised a qualitative ethnobotanical design using interviews, observations, and narrative analysis of indigenous curers to understand the use of medicinal plants and cultural significance. Results showed that herbal knowledge is well intertwined with communal identity, ecological adaptation,

where particular species are selected according to habitat and the healing tradition. Its advantage was the cultural verisimilitude and thorough contextualisation of local practise, but its weakness was the absence of biochemical confirmation of the connexion between traditional knowledge and quantifiable pharmacological activity. Based on these cultural observations, Nguyen et al. (2021) performed bioassays-directed extraction of herbs used in the traditional treatment of liver disorders and confirmed the anti-cytotoxic and anti-oxidant effects of *Hyptis suaveolens* and *Luvunga scandens*. The strength of the study was its ethnobotanical correspondence with traditional usage, but it did not provide clear records on the provenance of the plants or the ecology.

Conversely, Duong et al. (2023) used bioactive-guided isolation and molecular docking on *Dicranopteris linearis* and *Psychotria adenophylla*, linking their biochemical potency to environmental adaptation. Plants growing in wet lowlands had stronger ROS inhibition implying that ecological stress affects metabolite synthesis. Its strength was the combination of ecological sampling and compound-level analysis, but its drawback was a lack of discussion on sustainability. Likewise, Kim et al. (2020) tested *Peltophorum pterocarpum,* which have been traditionally grown in the Vietnamese tropical areas, with the help of ethanolic extracts confirming the presence of high cytotoxic and antioxidant activities. Although the study was able to validate a culturally relevant species, it did not take into account ecological management or long-term conservation. Collectively, these studies indicate that the ecological diversity and ethnomedical background in Vietnam are at the centre of the bioactive compound discovery. Nonetheless, the integration of cultural documentation, biodiversity mapping, and conservation-based research needs to be stronger in order to maintain therapeutic innovation and environmental integrity.

DISCUSSION

The reviewed studies collectively reveal that natural compounds from Vietnamese medicinal herbs demonstrate strong potential in targeting the interconnected mechanisms of cancer cell proliferation and cellular ageing. Flavonoids, terpenoids and phenolic derivatives consistently directed apoptosis regulation, oxidative stress equilibrium and mitochondrial stability, although they appear to act as multi-targeted pharmacological agents. The overlap of information provided by Tallei et al. (2025) and Kim et al. (2020) helps to confirm the idea that botanical compounds are regulating common signalling pathways, namely, p53, AKT1 and mTOR, which control tumour suppression and senescence. Moreover, the quantitative results of Nguyen et al. (2021) demonstrate that a high-level of flavonoid is associated with a higher cytotoxicity and antioxidant activity, which proves the biochemical association between polyphenolic density and therapeutic effect. Similarly, Duong et al. (2023) contributed to mechanistic knowledge by conducting molecular docking, which verifies the mechanism of enzyme inhibition in relation to oxidative ageing in silico. Nevertheless, in these studies, the methodological diversity, which goes as far as crude extract testing to isolating the compounds, makes cross-comparison and consistency challenging in interpreting potency. Nonetheless, the overall results of their research reinforce the hypothesis that the phytochemical complexity of Vietnamese herbs is the basis of their integrative anti-ageing and anticancer effects.

In addition, the nature of ecological variability and ethnobotanical tradition is revealed as a defining factor of therapeutic viability. The qualitative research presented by Muhajirin (2024) puts the context of how native knowledge guides the choice of plants that are further validated by modern pharmacological studies employing laboratory techniques. It is this convergence that makes the application of traditional insight and experimental science to increase credibility and sustainability important. In the meantime, the difference in bioactivity between habitats that was also evident in both Nguyen et al. (2021) and Duong et al. (2023) indicates that environmental stress and soil chemistry have a significant impact on the synthesis of phytochemicals. This mutual dependency indicates that preservation and minimal cultivation are more than ecological requirements they are also pharmacological requirements. Still, there is a lack of longitudinal or in vivo research to provide insights into safety, bioavailability, and dosage. Subsequently, standardised extraction protocols should be used, ecological mapping should be embraced and community-based conservation alliances should also be encouraged in the future to prevent erosion of traditional knowledge and facilitate scientific innovation. Collectively, these observations support the fact that Vietnamese medicinal herbs are

in a critical nexus of biology, ecology, and culture, and can be used to provide sustainable examples of building next-generation therapeutic agents against cancer and age-associated cellular ageing.

Limitations

The review had a number of limitations that affect the depth and generalisability of its findings. The greatest limitation was due to the heterogeneity of study designs because the examined studies varied in their approaches to extraction, concentrations of compounds, cell-line models, and endpoints of analysis and could not directly compare their findings. Numerous reports, such as Nguyen et al. (2021) and Kim et al. (2020) concentrated on in vitro experiments without further in vivo or clinical validation, translating only to therapeutic use. Likewise, the lack of standardisation of reporting of IC50 values, antioxidant indices, and molecular targets added variability, which decreased the interpretive precision. The other limitation was due to the lack of mechanistic exploration where only a couple of the studies, including that of Tallei et al. (2025) and Duong et al. (2023), have utilised molecular docking or pathway analysis, and thus gaps in the understanding of compound-protein interactions remain. Furthermore, ethnobotanical and ecological information were sporadically recorded, and it was not possible to evaluate the sustainability and context-specific effects. The bias in language also continued since there were only a few Vietnamese-language studies that were not translated and were not available in the international databases. As a result, the overall conclusions highlight a high level of bioactive potential, yet, the inconsistency in methodology, and inadequate mechanistic validation, as well as the lack of ecological aspects, limit the overall scientific generalisation of these encouraging findings and their applicability into practise.

Suggestions

Future research should adopt standardised experimental protocols for extraction, quantification, and biological testing to improve comparability and reproducibility across studies. Incorporating in vivo and clinical investigations will enhance understanding of pharmacokinetics, safety, and therapeutic effectiveness. Integrating multiomics and molecular docking approaches can clarify compound pathway interactions connecting ageing and cancer mechanisms (Wei et al. 2025). Researchers should also record ecological origins and ethnobotanical knowledge systematically to preserve cultural integrity and support sustainable use of natural resources (Dean 2024). Collaboration among scientists, local communities, and conservation institutions will be essential to translate Vietnam's plant diversity into validated therapeutic and environmentally responsible innovations.

CONCLUSION

The review came to the conclusion that Vietnamese medicinal herbs have been a crucial cross-linkage between cancer-inhibitory effects, cellular ageing regulation, and ecological diversity. In the reviewed literature, natural compounds, especially flavonoids, terpenoids, and phenolics, have been shown to be consistent in affecting apoptosis, oxidative stress, and mitochondrial activity, confirming their possible role in combined cancer and geroscience studies. Results have also indicated that ecological and traditional ethnobotanical practises are key contributors to compound potency and sustainability. Nonetheless, the lack of mechanistic detail, differences in extraction strategies, and a lack of in vivo validation limit direct clinical implementation. The future work will require strengthening the interdisciplinary cooperation of biologists, pharmacologists and ethnobotanists. In general, the Vietnam biodiversity and herbal knowledge offer a good basis to identify new therapeutics that would deal with ageing-related cancers and achieve environmental sustainability alongside cultural sustainability.

Declarations

- **Author Contribution Statement:** The author has made a substantial contribution to the conception, design, analysis, and writing of this review article.
- **Competing Interest Statement:** The author declares that there are no conflicts of interest regarding the publication of this paper.
- **Additional Information:** This article was thoroughly reviewed for clarity, structure, and grammatical accuracy by Claude.

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