revista de ciências da saúde NOVA ESPERANÇA VOLUME 24 ISSN ELETRÔNICO 2317-7160

ESSENTIAL OILS AND NEOPLASMS: EXPERIMENTAL EVIDENCE AND PERSPECTIVES IN CHEMOPROPHYLAXY AND INTEGRATIVE CHEMOTHERAPY

ÓLEOS ESSENCIAIS E NEOPLASIAS: EVIDÊNCIAS EXPERIMENTAIS E PERSPECTIVAS NA QUIMIOPROFILAXIA E QUIMIOTERAPIA INTEGRATIVA

Nathanaela Honório Paulino Batista dos Santos

Abstract. Neoplasms constitute a major public health challenge, with an increasing impact on morbidity and mortality, including in Brazilian regions such as the Northeast. In this context, complementary therapeutic strategies have been investigated to enhance the effectiveness of conventional treatments while reducing their adverse effects. Essential oils, natural compounds rich in bioactive volatile metabolites, have attracted growing scientific interest due to their anticarcinogenic and anticancer properties. This study aimed to analyze the scientific evidence regarding the role of essential oils and their major chemical constituents in cancer chemoprevention and integrative chemotherapy. This narrative integrative review was based on in vitro experimental studies and in vivo animal models investigating the molecular and cellular mechanisms underlying the antineoplastic activity of essential oils and their bioactive metabolites. The findings indicate that monoterpenes and sesquiterpenes, including citral, α-bisabolol, d-limonene, geraniol, β-elemene, diallyl trisulfide, and perillyl alcohol, are capable of inducing apoptosis, inhibiting cell proliferation, modulating tumor signaling pathways, interfering with angiogenesis, and enhancing the effects of conventional chemotherapeutic agents. Furthermore, selective cytotoxicity against tumor cells with reduced toxicity to normal cells has been observed in experimental models, representing a relevant advantage over traditional cytotoxic therapies. Despite these promising findings, the available evidence remains predominantly preclinical, highlighting the need for well-designed clinical trials to evaluate the safety, efficacy, dosage, route of administration, and clinical applicability of these compounds. It is concluded that essential oils have potential as complementary agents in integrative oncology and should be used cautiously and supported by robust scientific evidence.

Keywords: Aromatherapy; Carcinogenesis; Apoptosis. Natural Products; Integrative Oncology.

Resumo. As neoplasias constituem um importante problema de saúde pública, com impacto crescente na morbimortalidade, inclusive em regiões brasileiras como o Nordeste. Nesse contexto, estratégias terapêuticas complementares têm sido investigadas com o objetivo de ampliar a eficácia dos tratamentos convencionais e reduzir seus efeitos adversos. Os óleos essenciais, constituídos por metabólitos voláteis bioativos, vêm despertando interesse científico devido ao seu potencial anticarcinogênico e anticancerígeno. O presente estudo teve como objetivo analisar as evidências científicas acerca da atuação dos óleos essenciais e de seus principais constituintes químicos na quimioprevenção e como estratégias complementares no tratamento das neoplasias. Trata-se de uma revisão integrativa da literatura, fundamentada em estudos experimentais in vitro e modelos animais in vivo que investigaram os mecanismos moleculares e celulares envolvidos na ação antineoplásica de óleos essenciais e de seus metabólitos bioativos. Os resultados indicam que monoterpenos e sesquiterpenos, como citral, α-bisabolol, d-limoneno, geraniol, β-elemene, trissulfeto de dialilo e perilol, apresentam capacidade de induzir apoptose, inibir a proliferação celular, modular vias de sinalização tumoral, interferir na angiogênese e potencializar a ação de quimioterápicos convencionais. Observa-se, ainda, seletividade citotóxica em modelos experimentais, com menor citotoxicidade em células não tumorais, aspecto que representa um potencial diferencial em relação às terapias citotóxicas tradicionais. Apesar dos achados promissores, as evidências disponíveis concentram-se predominantemente em estudos pré-clínicos, indicando a necessidade de ensaios clínicos controlados que avaliem a segurança, a eficácia, a dose, a via de administração e a aplicabilidade desses compostos na prática assistencial. Conclui-se que os óleos essenciais apresentam potencial como agentes complementares na oncologia integrativa, devendo seu uso ser considerado de forma criteriosa e respaldada por evidências científicas.

Palavras-chave: Aromaterapia; Carcinogênese; Apoptose; Produtos naturais; Oncologia integrativa.

Curso de Enfermagem, Faculdade Nova Esperança (FACENE), João Pessoa, Paraíba, Brasil.
E-mail: nathanaelahonorio@gmail.com, 58068-330,
E-mail: nathanaelahonorio@gmail.com
CEP 58068-330, João Pessoa–PB, Brasil.
Currículo Lattes: http://lattes.cnpq.br/2299579461632953
ORCID iD: https://orcid.org/0009-0008-9667-6924)

Submissão: 07/02/2026 Aceite:02/07/2026
DOI: 10.17695/rcsne.vol24.n1.p120-129

INTRODUCTION

Neoplasms are considered one of the main causes of morbimortality in the world, posing an increasing challenge to the health systems[1]. In Brasil, a tendency for the progressive growth of mortality by cancer has been observed, even in states from the northeast, like Paraíba, in which recent analyses point to the consistent increase in mortality rates from neoplasms in both sexes, accompanied by a more rapid increase in females[2]. This scenery reinforces the neeed for theraupeutic strategies that not only amplify the efficacy of conventional treatments, but also contribute to the reduction of adverse effects and the enhancement in the quality of life for cancer patients.

Chemotherapy remains one of the main therapeautic modalities in cancer treatment, grounding its approach majorly in cytotoxic agents capable of interfering in the cellular cycle and inducing the death of tumor cells[3]. However, the low selectivity of these drugs frequently results in damage to healthy tissues, causing significant side effects, like immunosuppression, intense fatigue, hematologic changes, mucosal lesions and impairment of physical and emotional wellbeing[4].

Given those limitations, there has been a growing interest in integrative approaches which can act in a complementary manner, enhancing the antineoplastic activity and minimizing deleterious impacts of conventional treatments[5]. In this context, essential oils stand out as complex natural substances, composed predominantly of monoterpenes and sesquiterpenes, with recognized biological activity[6].

Experimental evidence exhibit that these compounds have distinct mechanisms of action compared to conventional chemotherapeutic agents, including modulation of cellular signaling pathways, selective induction of apoptosis, interference with tumor angiogenesis and enhancement of the response to chemotherapeutic agents[7]. Furthermore, some components of essential oils exhibit less toxicity toward normal cells, suggesting a promissing therapeutic profile in integrative oncology[8].

In line with this context, the present study aims to analyse the scientific evidence available regarding the performance of essential oils and their main chemical constituents in chemoprophylaxis and integrative chemotherapy of neoplasms[9].

MATERIALS AND METHODS

This is an integrative narrative review of a descriptive-analytical nature, conducted with the objective of gathering, critically analyzing, and synthesizing the scientific evidence available regarding the anticarcinogenic and anticancer potential of essential oils and its main chemical contituents, with an emphasis on its application in chemoprophylaxis and integrative chemotherapy for neoplasms[10].

The review was based on the analysis of experimental, translational, and clinical scientific studies, including in vitro trials done with human tumor cell lines, in vivo animal models with experimentally induced carcinogenesis, as well as data from observational clinical studies and preliminary trials[11]. Consideration was given to studies that investigated molecular, cellular and biochemical mechanisms involved in antineoplastic activity of essential oils and their volatile constituents, especially monoterpenes and sesquiterpenes[12].

The bibliographic research included national and international publications from scientific journals with recognized relevance in the field of Health Sciences, prioritizing articles indexed in widely used databases, like PubMed/MEDLINE, Scopus, Web of Science and ScienceDirect[13]. To identify the studies, descriptors selected from the Descritores em Ciências da Saúde (DeCS) and their English equivalents (Medical Subject Headings – MeSH) were used, combined via Boolean operators, including the terms essential oils, neoplasms, anticancer activity, integrative oncology, chemoprevention and apoptosis[14].

Although no strict timeframe was established, preference was given to studies published within the last five years, without limiting the inclusion of classic works considered fundamental to the understanding of the described mechanisms of action[15]. Studies presenting experimental data or consistent mechanistic analyses regarding the antineoplastic activity of essential oils were included, as well as relevant reviews that contributed to the consolidation of the state of the art on the theme. Publications containing insufficient information, lacking methodological clarity, or bearing no direct relation to the proposed objectives were excluded.

The analysis of the selected studies was conducted critically and comparatively, enabling the identification of recurring mechanisms of anticarcinogenic and anticancer activity, potential complementary therapeutic effects and existing gaps in scientific literature[16]. The results were organized in a thematic manner and discussed in light of available evidence, respecting the limitations inherent to the methodological design adopted.

In addition, secondary data regarding death from neoplasms was used for epidemiological context of the research problem. The informations were obtained from the Mortality Information System (SIM), made available by the Department of Informatics of the Unified Health System (DATASUS), through the platform TABNET, considering deaths by residency classified under Chapter II of the International Classification of Deseases – ICD-10 (Neoplasms)[17]. The data cover the period from 2019 to 2024, stratified by sex for the state of Paraíba, using final data up to 2023 and preliminary data for the year 2024. For the calculation of death rates, population projections from the Brazilian Institute of Geography and Statistics (IBGE)[18] were used. The analysis of the data was conducted descriptively, with a graphical presentation of temporal trends and without the application of inferential statistical tests, with the aim to support the contextualization of the impact of neoplasms in the regional setting.

RESULTS AND DISCUSSION

The analysed studies demonstrate that essential oils and their main chemical constituents present a diversified set of anticarcinogenic and anticancer mechanisms, acting at different stages of carcinogenesis and tumor progression[19]. These effects involve, mainly, the modulation of oxidative stress, selective induction of apoptosis, inhibition of cell proliferation, interferance in tumoral signaling pathways and angiogenesis modulation, acting as potential agents in the context of integrative oncology[20].

Experimental evidence of antineoplastic potencial of essential oils

The Table 1 synthesizes the main compounds of essention oils described in scientific literature with antineoplastic activity, highlighting their chemical classification, pharmacological effects, experimental models used and corresponding references[21]. It is observed that monoterpenes and sesquiterpenes constitute the prominent class amidst the investigated constituents, which reinforces the relevance of these secondary metabolites in the development of complementary therapeutic strategies.

TABLE 1 – Constituents of essential oils with antineoplastic potential, pharmalogical effects and experimental models used.

Constituent / Essential oil	Chemical classification	Antineoplastic effect	Experimental model	Reference
Citral	Monoterpene	Glutatione-S-transferase (GSTP1) induction, anticarcinogenic activity	Rats (in vivo)	Nakamura et al.
α-Bisabolol	Sesquiterpenoid Alcohol	Selective induction of apoptosis in glioma cells	Tumor cell cultures and animal models	Cavalieri et al.

Constituent / Essential oil	Chemical classification	Antineoplastic effect	Experimental model	Reference
β-Elemene	Sesquiterpene hydrocarbon	Increase in glioma survival	Clinical data from patients	Tan et al.
Geraniol	Monoterpenoid alcohol	Inhibition of thymidine synthase and thymidine kinase; enhancement of 5-fluorouracil	Colon cancer cells and mice with xenograft	Carnesecchia et al.; Mans et al.
d-Limonene	Monoterpene	Anti-angiogenic and pro-apoptotic activity, inhibition of farnesyltransferase	In vitro and in vivo models	Guang et al.; Kaji et al.; Srinivas
Diallyl Trisulfide (DATS)	Organosulfur	Cell cycle arrest in the G2/M phase and apoptosis induction	Human hepatic tumor cells	Wu et al.; Thomson & Ali
Perillyl alcohol	Hydroxylated monoterpene	Inhibition of angiogenesis and apoptosis induction	Diverse tumor models	Loutrari et al.
Melissa officinalis	Complete essential oil	Cytotoxicity in multiple tumor lines	Human and murine cell lines	De Sousa et al.

Source: Adapted from Edris AE. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. Phytother Res. 2007;21(4):308–323.

Citral demonstrated the capacity to induce the expression of phase II enzymes, like glutatione-S-transferase, favoring cellular detoxication processess and reducing formation of mutagenic agents[22]. The α-bisabolol stood out due to the selective induction of apoptosis in glioma cells, with less impact on normal cells, a feature considered advantageous compared to traditional cytotoxic chemotherapy drugs[23].

β-elemene presented translational relevance demonstrated by increased survival in patients with gliomas, while being one of the few constituents of essential oils with associated clinical evidence[24]. Geraniol demonstrated acting like a tumor sensitizer, inhibiting enzymes related to chemotherapy resistence, enhancing fluoruracil activity[25]. In a similar manner, d-limonene demonstrated anti-angiogenic and pro-apoptotic properties, in addition to interfering in protein activation involved in tumor progression[26].

Organosulfur compounds like diallyl trisulfide presented capacity of blocking the cell cycle in the G2/M phase and inducing apoptosis in human hepatic tumor cells [27]. Perillyl alcohol and Melissa officinalis essential oil demonstrated cytotoxicity in multiple tumor cell lines, suggesting a spectrum of activity that is broad and unrestricted to only one type of neoplasm[28].

Molecular mechanisms involved in antineoplastic activity

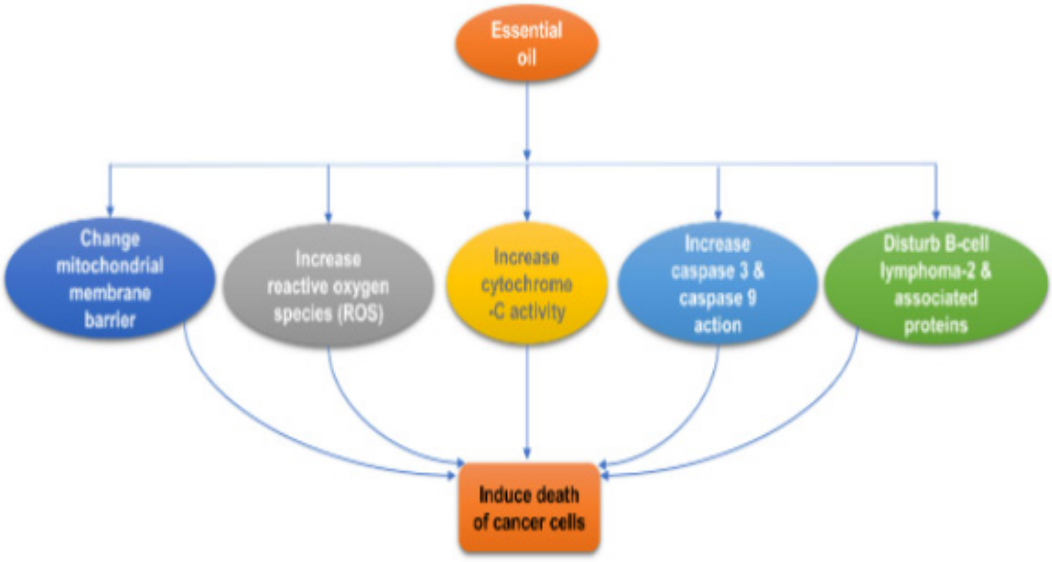
The anticarcinogenic mechanisms attributed to essential oils are synthesized in Figure 1, which represents its activity in tumor chemoprophylaxis, including the inhibition of carcinogen-activating enzymes, reduction in the formation of mutagenic metabolites, modulation of oxidative stress and induction of detoxification enzyme systems[29].

FIGURE 1 – Anticarcinogenic mechanisms of essential oils in tumor chemoprophylaxy.

Source: Adapted from Kashyap (2024).

Meanwhile, Figure 2 illustrates the main molecular mechanisms associated with anticancer activity of essential oils in established neoplasm cells, emphasizing alteration in mitochondrial permeability, increase in the production of reactive oxygen species, release of cytochrome-c and the activation of caspases, culminating in cellular apoptosis[30]. These mechanisms differ, partially, from those observed in conventional chemotherapy, which may explain the lower relative toxicity observed in experimental models[31].

FIGURE 2 – Main molecular mechanisms involved in the anticancer activity of essential oils.

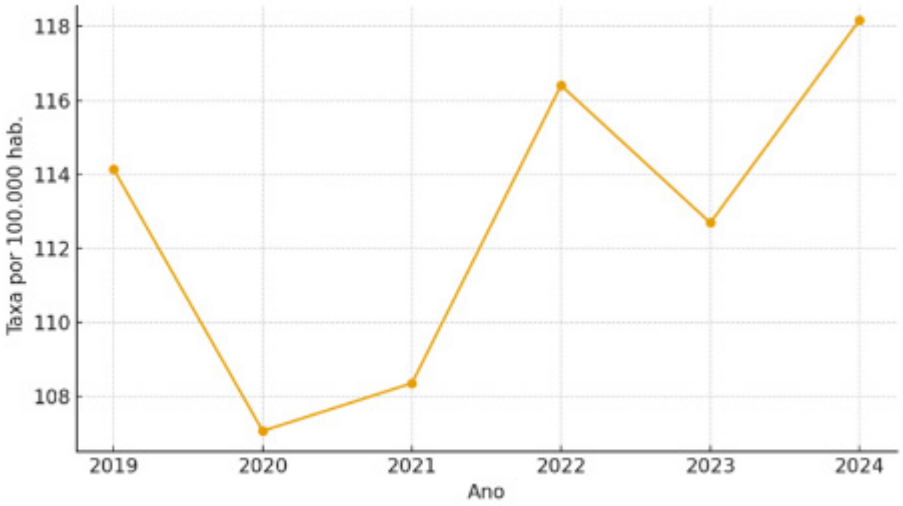


Source: Adapted from Kashyap (2024).

Epidemiological context of neoplasms

The analysis of secondary mortality data from neoplasms in the state of Paraíba, during the period of 2019 to 2024, highlights the magnitude of cancer as a public health issue in the regional scene[32]. Figure 3 shows that mortality from neoplasms in males has had a growth tendency during the analized period, even with interannual variations, possibly related to differences in the incidence profile, late diagnosis and access to health services[33].

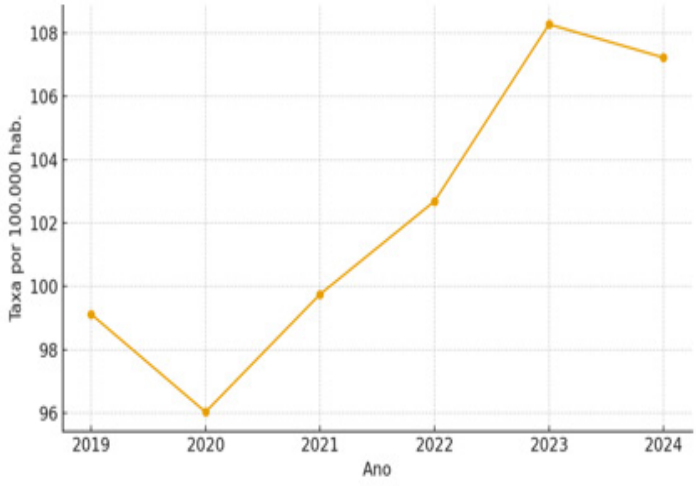
FIGURE 3 – Mortality rate from neoplasms in males. Paraíba, 2019–2024.



Source: Mortality Information System (SIM/DATASUS); Brazilian Institute of Geography and Statistics (IBGE).

Figura 4 demonstrates that mortality from neoplasms in females has had a more consistent and progressive growth, suggesting more stability in the temporal trend[34]. This pattern may be associated with the incidence of hormone-dependent cancers, population aging and environmental and behavioral factors, emphasizing the need for continuous strategies of prevention and treatment.

FIGURE 4 – Mortality rate from neoplasms in females. Paraíba, 2019–2024.



Source: Mortality Information System (SIM/DATASUS); Brazilian Institute of Geography and Statistics (IBGE).

Clinical relevance and implications for integrative oncology

The epidemiological findings reinforce the need for therapeutic approaches that go beyong the cytotoxic model exclusively, incorporating complementary strategies capable of acting in prevention as well as in neoplasm treatment[35]. In this context, the experimental results presented in this review indicate that essential oils can play a relevant role as supporting agents in integrative oncology, contributing to the potentiation of chemotherapy and the reduction of adverse effects[36].

The analysis of secondary data about death from neoplasms in the state of Paraíba, during the period of 2019 to 2024, shows the magnitude and epidemiological relevance of cancer as a public health issue in the region[37]. The mortality rates were analysed in a descriptive manner, stratified by sex, making it possible to identify distinct temporal trends between men and women[38].

As shown in Figure 3, it is evident that mortality from neoplasms in males has had a tendency of growth during the analysed period, although with more variability among the years[39]. This oscilation may reflect differences is the distribution of types of cancer, in the access of health services, in late diagnosis and in response to treatment, aspects frequently associated to a male epidemiological profile. Nevertheless, the ascending rate behaviour reinforces the persistence of neoplasm as a relevant cause of mortality in this population.

On the other hand, Figure 4 demonstrates that mortality from neoplasms in females has had more consistent and progressive growth along the analyzed years[40]. The observed tendency suggests more stability in the growth rate, which can be related to incidence of hormone-dependent cancers, to population aging and factors associated with lifestyle and environmental conditions.

These epidemiological findings reinforce the urgency of therapeutical approaches that go beyong the cytotoxic model exclusively, incorporating complementary strategies capable of acting in prevention as well as in neoplasm treatment[41]. In this context, the experimental results presented on Table 1 gain relevance, demonstrating that essential oils and its chemical constituents have biological mechanisms capable of interfering in fundamental processes of carcinogenesis and tumor progression[42]. The integration between the regional epidemiological scenery and the mechanistic evidence described in scientific literature strengthens the relevance of integrative oncology as a promissing field in health care, especially when guided by a solid scientific foundation[43].

CONCLUSION

The analysed scientific evidence in this integrative review point that essential oils and its main chemical contituents present relevant anticarcinogenic and anticancer potential, acting through multiple biological mechanisms, like selective induction of apoptosis, modulation of tumoral signaling pathways, interference in angiogenesis and potentiation of the actions of conventional chemotherapeutic agents[44]. These mechanisms differ, partially, from those observed in classic cytotoxic drugs, suggesting a promissing complementary therapeutic profile in the context of integrative oncology.

The epidemiological analysis of mortality from neoplasms in the state of Paraíba reinforces the magnitude of cancer as a public health issue, and emphasizes the need for therapeutic strategies that transcend exclusively the cytotoxic model[45]. In this scenery, essential oils emerge as potential complementary tools in chemoprophylaxis as well as in care during chemotherapy, as long as its use is fundamented in scientific evidence and integrated with conventional practices in an ethical and rigorous manner.

Despite the promissing results observed in experimental studies and in preliminary clinical evidence, it is worth noting that most of the scientific findings are still concentrated in preclinical models, which limits direct extrapolation to healthcare practice[46]. Therefore, it is essential to make controlled clinical trials, translational studies and systematic reviews that consolidate safety, efficacy and usage protocols of essential oils in oncology.

In conclusion, essential oils possess potential as complementary agents in oncology care, contributing to approaches that are more integrative, human and patient-centered. Their incorporation in health practices must be guided by interdisciplinarity, scientific rigor and adequate professional training, especially in Nursing and Integrative and Complementary Health Practices[47].

REFERENCE

1. Edris AE. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. Phytother Res. 2007;21(4):308–323.
2. Kashyap R. Exploring molecular mechanisms and therapeutic potential of essential oils: a systems biology approach. Future Integr Med. 2024;3(2):116–131.
3. Agarwal P, Sebghatollahi Z, Kamal M, et al. Citrus essential oils in aromatherapy: therapeutic effects and mechanisms. Antioxidants (Basel). 2022;11(12):2374.
4. Brito AMG, Rodrigues SA, Brito RG, Xavier-Filho L. Aromaterapia: da gênese à atualidade. Rev Bras Plantas Med. 2013;15(4):789–793.
5. World Health Organization. Cancer. Geneva: WHO; 2023.
6. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17–48.
7. Brasil. Ministério da Saúde. Sistema de Informações sobre Mortalidade (SIM). Brasília: Ministério da Saúde; 2024.
8. Instituto Brasileiro de Geografia e Estatística (IBGE). Projeções da população do Brasil e Unidades da Federação. Rio de Janeiro: IBGE; 2024.
9. De Sousa DP. Bioactive essential oils and cancer. Curr Pharm Des. 2017;23(10):1531–1541.
10. Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis. Am J Epidemiol. 1992;136(10):1184–1203.
11. Nakamura Y, Miyoshi N, Isemura M. Dietary phytochemicals for cancer prevention: effects of citral on phase II detoxifying enzymes. Cancer Lett. 2003;190(1):9–16.
12. Cavalieri E, Bergamini C, Mari M, et al. Involvement of mitochondrial permeability transition pore opening in alpha-bisabolol induced apoptosis. FEBS Lett. 2004;576(1–2):87–90.
13. Tan W, Lu J, Huang M, et al. Anti-cancer natural products isolated from Chinese medicinal herbs. Chin Med. 2000;3:1–15.
14. Carnesecchi S, Langley K, Exinger F, et al. Geraniol sensitizes human colon cancer cells to 5-fluorouracil. J Pharmacol Exp Ther. 2004;310(2):625–632.
15. Mans DR, et al. Effects of geraniol on thymidylate synthase activity. Cancer Chemother Pharmacol. 1999;43(6):511–517.
16. Kaji I, Tatsuta M, Iishi H, et al. Inhibition of hepatocarcinogenesis by d-limonene. Cancer Lett. 2001;172(2):185–192.
17. Srinivas PR, et al. Inhibition of protein prenylation by monoterpenes. Cancer Res. 1986;46(12):6190–6194.
18. Loutrari H, et al. Perillyl alcohol is an angiogenesis inhibitor. J Pharmacol Exp Ther. 2004;311(2):568–575.
19. Wu PP, et al. Diallyl trisulfide induces cell cycle arrest and apoptosis. Mol Cancer Ther. 2004;3(9):1041–1049.
20. Thomson M, Ali M. Garlic as an anti-cancer agent. Curr Cancer Drug Targets. 2003;3(1):67–81.
21. De Sousa DP, et al. Antitumor activity of Melissa officinalis essential oil. Fitoterapia. 2004;75(2):112–116.
22. Legault J, Pichette A. Potentiating effect of beta-caryophyllene on anticancer drugs. J Pharm Pharmacol. 2007;59(12):1643–1647.
23. Modzelewska A, Sur S, Kumar SK, Khan SR. Sesquiterpenes as anticancer agents. Bioorg Med Chem. 2005;13(9):3147–3155.
24. Wang G, Li X, Huang F, et al. β-elemene induces apoptosis in glioma cells. J Neurooncol. 2005;72(3):243–249.

10. Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis. Am J Epidemiol. 1992;136(10):1184–1203.
11. Nakamura Y, Miyoshi N, Isemura M. Dietary phytochemicals for cancer prevention: effects of citral on phase II detoxifying enzymes. Cancer Lett. 2003;190(1):9–16.
12. Cavalieri E, Bergamini C, Mari M, et al. Involvement of mitochondrial permeability transition pore opening in alpha-bisabolol induced apoptosis. FEBS Lett. 2004;576(1–2):87–90.
13. Tan W, Lu J, Huang M, et al. Anti-cancer natural products isolated from Chinese medicinal herbs. Chin Med. 2000;3:1–15.
14. Carnesecchi S, Langley K, Exinger F, et al. Geraniol sensitizes human colon cancer cells to 5-fluorouracil. J Pharmacol Exp Ther. 2004;310(2):625–632.
15. Mans DR, et al. Effects of geraniol on thymidylate synthase activity. Cancer Chemother Pharmacol. 1999;43(6):511–517.
16. Kaji I, Tatsuta M, Iishi H, et al. Inhibition of hepatocarcinogenesis by d-limonene. Cancer Lett. 2001;172(2):185–192.
17. Srinivas PR, et al. Inhibition of protein prenylation by monoterpenes. Cancer Res. 1986;46(12):6190–6194.
18. Loutrari H, et al. Perillyl alcohol is an angiogenesis inhibitor. J Pharmacol Exp Ther. 2004;311(2):568–575.
19. Wu PP, et al. Diallyl trisulfide induces cell cycle arrest and apoptosis. Mol Cancer Ther. 2004;3(9):1041–1049.
20. Thomson M, Ali M. Garlic as an anti-cancer agent. Curr Cancer Drug Targets. 2003;3(1):67–81.
21. De Sousa DP, et al. Antitumor activity of Melissa officinalis essential oil. Fitoterapia. 2004;75(2):112–116.
22. Legault J, Pichette A. Potentiating effect of beta-caryophyllene on anticancer drugs. J Pharm Pharmacol. 2007;59(12):1643–1647.
23. Modzelewska A, Sur S, Kumar SK, Khan SR. Sesquiterpenes as anticancer agents. Bioorg Med Chem. 2005;13(9):3147–3155.
24. Wang G, Li X, Huang F, et al. β-elemene induces apoptosis in glioma cells. J Neurooncol. 2005;72(3):243–249.
25. Zhang Y, et al. Clinical application of β-elemene in cancer therapy. Oncol Lett. 2018;15(6):9361–9366.
26. Rehman MU, et al. Apoptosis signaling pathways in cancer. Oncol Rev. 2017;11(1):327.
27. Fulda S, Debatin KM. Extrinsic versus intrinsic apoptosis pathways. Oncogene. 2006;25(34):4798–4811.
28. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674.
29. Aggarwal BB, et al. Molecular targets of nutraceuticals. Biochem Pharmacol. 2006;71(10):1397–1421.
30. Green DR, Kroemer G. The pathophysiology of mitochondrial cell death. Science. 2004;305(5684):626–629.
31. Fulda S. Modulation of apoptosis by natural products. Nat Prod Rep. 2014;31(4):504–516.
32. Brasil. DATASUS. TABNET: Mortalidade por neoplasias (CID-10). Brasília: Ministério da Saúde; 2024.
33. Torre LA, et al. Global cancer incidence and mortality. CA Cancer J Clin. 2020;70(1):7–30.
34. Sung H, et al. Global cancer statistics 2021. CA Cancer J Clin. 2021;71(3):209–249.
35. Frenkel M, et al. Integrative oncology. CA Cancer J Clin. 2012;62(5):325–345.
36. Deng G, Cassileth BR. Integrative oncology: complementary therapies. CA Cancer J Clin. 2013;63(2):109–127.
37. Ministério da Saúde. Política Nacional de Práticas Integrativas e Complementares. Brasília; 2018.
38. Tesser CD, et al. Práticas integrativas na atenção à saúde. Saude Soc. 2019;28(3):174–188.
39. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33.
40. Bray F, et al. Global cancer transitions. Lancet Oncol. 2018;19(4):531–542.
41. Repetto G, et al. Toxicity screening of natural products. Food Chem Toxicol. 2008;46(1):23–31.
42. Cragg GM, Newman DJ. Natural products as sources of anticancer agents. J Ethnopharmacol. 2005;100(1–2):72–79.
43. Newman DJ, Cragg GM. Natural products as drugs. J Nat Prod. 2020;83(3):770–803.

44. De la Torre Torres JE, et al. Essential oils and apoptosis. Phytomedicine. 2019;58:152870.
45. Organização Pan-Americana da Saúde. Câncer nas Américas. Brasília: OPAS; 2023.
46. Atanasov AG, et al. Discovery and resupply of pharmacologically active natural products. Biotechnol Adv. 2015;33(8):1582–1614.
47. World Health Organization. WHO global report on traditional and complementary medicine. Geneva: WHO; 2019.
48. Dudai N, Weinstein Y, Krup M, Rabinski T, Ofir R. Citral is a new inducer of caspase-3 in tumor cell lines. Planta Med. 2005;71(5):484-488.
49. Yao YQ, Ding X, Jia YC, Huang CX, Wang YZ, Xu YH. Anti-tumor effect of beta-elemene in glioblastoma cells depends on p38 MAPK activation. Cancer Lett. 2008;264(1):127-134.
50. Crowell PL. Prevention and therapy of cancer by dietary monoterpenes. J Nutr. 1999;129(3):775S-778S.