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Review Article

Traditional and contemporary herbal medicines in management of cancer: A scoping review

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ABSTRACT

Background: Cancer is one of the leading causes of death worldwide and is primarily managed by chemotherapy, radiation and surgery. Traditional medicine is widely used worldwide due to availability, affordability, wide applicability and accessibility. While potential for traditional medicines in management of cancer is well-documented, there is limited literature that collates traditional knowledge and contemporary herbal medicine practice.

To collate available evidence on herbal medicines used in the management of all cancers from traditional world-wide sources, and the management of lung and colorectal cancers in contemporary practice.

Medicinal plants with anti-cancer properties were identified following JBI methodology for scoping reviews through searches of the following sources: Trove, Archive.Org, and Henriette's herbal medicine page (traditional texts), book list available from World Naturopathic Federation white paper (contemporary naturopathic texts), and in PubMed, MEDLINE, SCOPUS, ScienceDirect, AMED and JSTOR (case studies).

Of the 1973 citations retrieved, 38 traditional texts, 3 contemporary naturopathic texts and 10 case studies were included in the review. The traditional texts (n = 110) noted the highest number of different anti-cancer herbal species, followed by case reports (n = 52) and contemporary texts (n = 13).

This review identified various herbal medicines used to treat cancer traditionally which is distinct to those found in contemporary use. Moreover, this review identified the use of herbs from other native medical systems around the world in the contemporary naturopathic practice and individual case management. The evidence presented in the review could be utilized in pre-clinical settings to research traditional preparations of herbs.

1. Introduction

Cancer is a major public health concern and is the leading cause of mortality and morbidity worldwide, with approximately 10 million deaths in 2020, primarily caused by lung, colorectal, liver, stomach and breast cancer [1]. Breast, lung and colorectal are likely to continue to rise with number of new cases expected to increase to 23.5 million by 2030 [2].

Mainstream treatment approaches for cancer include surgery, chemotherapy and radiation, with chemotherapy that benefits patients by reducing relapse and metastasis and increasing overall survival [3]. While a range of cytotoxic chemotherapeutic agents, including alkylating agents, anti-metabolites, anti-tumor antibiotics, topoisomerase inhibitors, and tubulin-binding drugs that target multiple cancer mechanisms to disrupt cell cycle are widely used [4], they tend to drive the poly-pharmacy approach to cancer management. This approach can lead to increase in side effects which in turn creates the need to develop new, more targeted approaches to cancer treatment.

Herbal medicines and traditional knowledge offer a new and attractive option to search for new potential chemotherapies. It is estimated that approximately 70,000 plant species have traditionally been used for medicinal purposes, and over 3000 species may have potential anti-cancer properties [1,1,5]. Indeed, over 60% of currently used chemotherapy agents, including paclitaxel, vincristine, vinblastine, etoposide, irinotecan and topotecan, are plant-derived and are currently used in clinical settings [6]. In contemporary healthcare settings, traditional medicine practitioners, herbalists and naturopaths use herbs, herbal extracts and preparations to complement current medical treatment and promote general wellbeing. These practitioners also play an important role in managing disease for patients with reduced

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accessibility to conventional treatment and/or medical facilities and patients who decline medical treatment approaches [7].

Traditional systems use a holistic approach to health and disease and often utilize whole plant or a combination of plants/herbal extracts as treatment preparation. Phytochemicals, the biologically-active plant secondary metabolites present in roots, leaves, flowers, stems and bark can perform several pharmacological functions in the human systems [8]. These phytochemicals act by regulating molecular pathways which have been implicated in carcinogenesis [8], including increasing antioxidant status, carcinogen inactivation, inhibiting proliferation, induction of cell cycle arrest and apoptosis, inhibition of metastasis of cancer cells and regulation of the immune system [9]. Phytochemicals with anti-cancer properties that have been studied in cellular and animal models include curcumin *(Curcuma longa),* allicin (*Allium sativum*), alpinumisoflavone (*Derris eriocarpa*), resveratrol (*Polygonum cuspidatum*), and thymoquinone (*Nigella sativa*) [10–12].

The present scoping review is aimed at synthesizing traditional and contemporary herbal knowledge with specific focus on aligning herbal/plant part and preparation(s) used with symptom(s) and/or overall cancer management. Traditional texts screened for this review did not differentiate between cancers, but due to the high number of different cancer types only two cancer types were chosen for scoping of the contemporary texts and case studies. Lung and colorectal cancers caused 1.80 million deaths and 916,000 deaths in 2020 [13] and naturopaths and herbal medicine practitioners reportedly manage active, malignant cancer, and provide care for post-cancer recovery, support and prevention, and treatment side effects [14]. Therefore, this scoping review synthesized herbal medicines and phytocompounds used in the management of cancer as recorded in traditional (all cancers) and contemporary texts and case studies (lung and colorectal cancers). This synthesis may guide future investigation of possible anti-cancer properties of herbal preparations and compounds.

2. Methods

2.1. Protocol

A scoping review was conducted in accordance with Joanna Briggs Institute methodology (JBI) [2] and the protocol was registered with the Open Science Framework (https://doi.org/10.17605/OSF.IO/4QCZS). The findings are reported using the suggested items provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for scoping reviews (PRISMA-ScR) [15].

2.2. Information sources

Traditional texts were searched using Henriette's Herbal medicine page, Trove and Archive.org. Contemporary text selection was guided by the World Naturopathic Federation (WNF) book list for their proximity and strong working relationship with the World Health Organization (WHO) and oversight of the global naturopathic practice. Additional contemporary texts were identified through manual and hand searching. The published peer-reviewed case studies were searched through the accessible electronic databases: PubMed, MEDLINE (EBSCO), AMED, SCOPUS. Case studies published in traditional texts were identified through hand searching of Henriette's Herbal medicine page.

2.3. Search strategy

To search for traditional herbs used in cancer management search terminology for 'cancer' that aligns with traditional sources was firstly identified. To achieve this, a preliminary search of the relevant articles using an electronic database search of PubMed, MEDLINE, SCOPUS, ScienceDirect, JSTOR and Google Scholar was conducted, and these terms with explanations can be found in Supplemental file 1. The search strategy for traditional texts was developed using the following identified terms; Carcinoma, Chancre, Carcinomata, Carcinodes, Canker, Karkinos, Cancer, Cancre, Cancor, Carcinos, Cacoethes, Cancroid, Chancroid, Kakoethes, Scirrhus, Struma, Carcinode, Kanker, Karkinomata, Tumour and Tumor.

Separate search strategies for contemporary texts and case studies were developed using MeSH terms for 'contemporary medicine', and 'cancer'. The Boolean operators OR and AND were used within and between categories respectively. Full methods with search strategies are presented in the registered protocol [16] and Supplemental file 2.

2.4. Study Selection Process

The inclusion criteria included texts from any country and setting but written and published in English or could be translated to English as well as texts and case studies with the primary focus on cancer and herbal medicine with publication date for study and texts inclusion of: 1800 to 1945 (traditional texts), 1945 to now (contemporary naturopathic texts). Types of study designs included: primary research studies (qualitative and quantitative), systematic reviews, meta-analyses, literature reviews, editorials, books, book chapters, naturopathic websites and blogs, herbal medicine websites, case reports, case studies, white papers, and other grey literature.

Exclusion criteria excluded texts not accessible online, no clear reference to the use of medicinal herbs, cancers in animals or animal models and metastatic cancers.

All identified citations, traditional and contemporary texts and case studies were exported to EndNote X9/2020 (Clarivate Analytics, PA, USA) in separate libraries. Duplicates were removed and titles and abstracts from all libraries were reviewed. Two reviewers independently checked the initial titles and abstract screening and excluded relevant citations (II, AB). Potential full text articles were retrieved, and the manuscripts imported. The full text of selected articles was assessed in detail against inclusion criteria (II) and checked (AB, JS). Reasons for exclusion were recorded and disagreements between reviewers during the selection process were resolved through discussion. PRISMA diagram was generated using JBI template (Fig. 1).

2.5. Data extraction

Excerpts from each of the information sources were identified as data when organizing into extraction tables, one for each for traditional texts, contemporary texts, and case studies. The data extraction table from traditional and contemporary sources included: information source (citation, country of publication or publisher), methods (cancer of interest, botanical name and common name, plant part used, preparation method, dosage, administration method, single/multiple herb remedy) and symptom treated. In addition to this, data extracted from traditional texts also included terminology used to identify the data point and was sorted by cancer type and body system. The data extraction table for peer-reviewed case studies was modified to include the treatment plan (integrative treatment) and patient outcomes of the treatment in contrast to 'symptom treated' in traditional texts.

The extracted data was entered into the NVivo 12/2018 (QSR International) software and coded into representative themes: common cancer type, herbal medicine used, common preparation type, plant part used, and expected outcome across the time periods.

3. Results

The literature search yielded a total of 1973 citations with 1958 from databases and 15 from hand searching (Fig. 1). Following removal of duplicates, 1966 texts and articles were included for screening. Texts and articles (title and abstract for case studies) that did not meet the inclusion criteria were removed (n = 1804), and a total of 162 texts and articles were screened for eligibility. After full text review for eligibility,

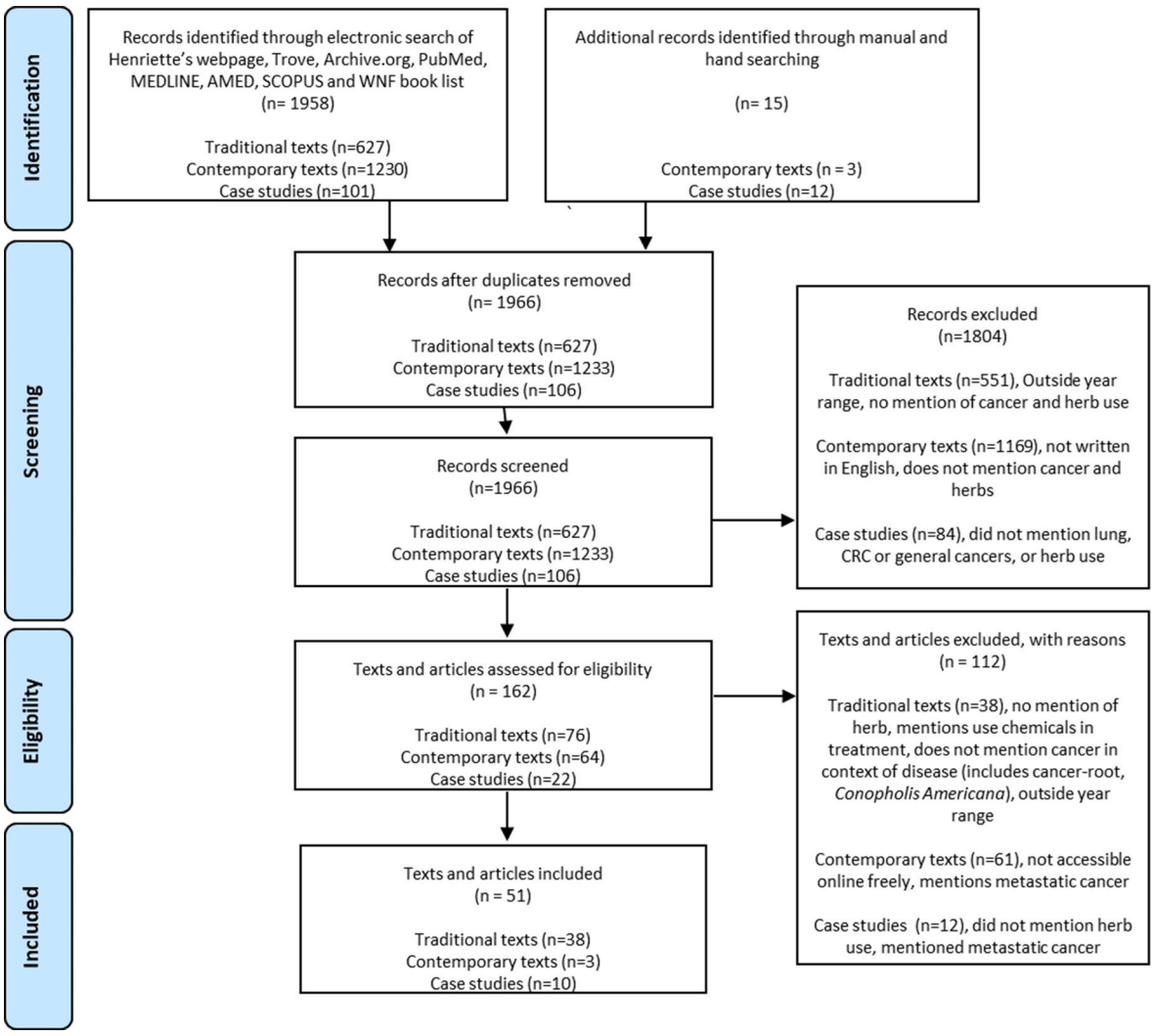

Fig. 1. Study selection process (modified PRISMA-ScR Flow Chart).

a total of 51 texts and articles were included for data extraction. Final data set comprised of 38 traditional texts, 3 contemporary naturopathic texts and 10 case studies.

3.1. Herbal medicines from traditional texts

This scoping review included 38 traditional texts published between 1800 and 1900 (n = 19) and from 1901 to 1945 (n = 19). Most texts were published in North America (n = 32) while remaining texts originated in Great Britain (n = 5) and Germany (n = 1) (Table 1). The most common terms used to define or indicate cancer across all the traditional texts included cancer (53.0%), tumor (14.2%) and carcinoma (10.8%) (Table 1).

Total of 194 herbal entries were identified with the highest number of herbal entries recorded in the *King's American Dispensary* [17] (n = 34) and equal number of herbal entries (n = 20) mentioned in *Excerpt from Boericke's Materia Medica: The Tinctures* [18] and *The American Materia Medica, Therapeutics and Pharmacognosy* [19].

99 herbal entries (50.8%) were used to manage cancer where the type of cancer treated was not specified. Of the system-specific cancers, herbs managing the reproductive system (21.5%), including breast, cervix, uterus, and testes, and digestive cancers (19.0%), including stomach, liver, intestine, rectum and mouth, were most represented. Only two herbs (1.0%) identified were linked to managing respiratory, visual and lymphatic cancers (Table 1).

Table 1
Study characteristics.

Publication Year	Number of Texts
1800–1850	19
1851–1900	12
1901–1945	7
Country of Publication	**Number of Texts**
North America	32
Britain	5
Germany	1
Cancer Terminology	**Percentage of Mention[a] (%)**
Cancer	53
Tumor, Tumour	14
Carcinoma	11
Other	2
Cancer Type	**Percentage of Mention[b] (%)**
General	51
Reproductive	21
Digestive	19
Integumentary	4
Urinary	2
Lymphatic	1
Respiratory	1
Visual	1

[a] Values are expressed as percentage mention of specific cancer term from total cancer terms; total cancer terms: n = 231.
[b] Values are expressed as percentage mention of cancer of interest from total cancer types; total cancer types: n = 194.

195 herb entries mentioned 110 individual herb species for cancer management from 1800 to 1945 across all 38 traditional texts (Supplemental file 3). *Hydrastis canadensis* (n = 16), *Echinacea angustifolia* (n = 13), *Thuja occidentalis* (n = 10), *Phytolacca* sp.; *decandra, Phytolacca Americana* (n = 9), *Trifolium pretense* (n = 8), *Chelidonium majus* (n = 7), *Conium maculatum* (n = 7), *Sanguinaria canadensis* (n = 7), *Calendula officinalis* (n = 7) and the fungus *Claviceps purpurea* (n = 6) were the most common, while multiple herbs including *Apium* sp. (n = 1) and *Apoycnum* sp. (n = 1) received the least mentions in this data set (Fig. 2).

Roots and rhizomes (17.1%) were the most commonly mentioned plant parts used for herbal preparation. Other plant parts of medicinal herbs used included leaves (12.6%), bark (8.1%), flowers and blossoms (5.0%), fruit and seed (5.0%), oil and resin (3.6%) (Fig. 3). Herbal preparations of *Achillea millefolium, Salvia miltiorrhiza, Ballota nigra, Lobelia inflata, Orobanche virginiana, Oxalis acetosella, Solanum dulcamara, Epiphegus virginiana, Galium aparine, Phytolacca Americana and Rumex Acetosella* included use of the whole plant (5.0%) (Supplemental file 3). Of the 195 herb entries, 162 were used as single (83.0%), and 28 in multiple (14.4%) preparations. Only *Thuja occidentalis* was found to be administered as both in single and mixed preparations (0.5%) and further four entries (2.1%) did not specify preparation mix (Fig. 3).

Fluid extracts were the most commonly found herbal preparation method (15.8%), followed by tincture (14.8%), specific medicine (9.4%), ointment (9.1%), infusion (8.4%), decoction (6.1%) and poultice (5.1%) (Fig. 3). Scudder (1870) [20] defines specific medicine as, "*we use the term* **specific** *with relation to definite pathological conditions, and propose to say, that certain well determined deviations from the healthy state, will always be corrected by certain specific medicines*", and this term is frequently used in North American traditional texts prior to 1922.

Most herbal preparations were administered internally (35.6%) as a fluid extract, decoction, infusion, pills, syrups or injections. Some preparations are administered externally (29.9%) in the form of a poultice, plaster, ointment or liniment (Fig. 3). Certain herbs such as *Gossypium herbaceum, Calendula officinalis,* and *Phytolacca americana* were administered both internally and externally (11.9%). The herbs were administered in doses of Oj (1 pint = 20 fl oz), ℨviij (8 troy ounces = 0.44 fl oz), ʒss (½ drachm = 0.03 oz), ℿi (1 minim = 0.002 fl oz), gtts. Ij (2 drops) and grs. x. (10 grains = 0.18 oz). A troy ounce was specific metric to measure weight of precious metal in the Middle Ages with one troy ounce equivalent to 0.055 Fl oz or 31.10 g.

Traditional medicinal herbs such as *Hydrastis Canadensis* (single and mixed preparations), *Conium maculatum, Trifolium pratense, Thuja occidentalis, Baptisia tinctoria, Sanguinaria canadensis, Phytolacca decandra, Claviceps purpurea, Echinacea* sp. *Carica papaya, Chelone glabra, Corallium rubrum, Daucus carota, Epifagus virginiana, Lamiastrum galeobolon, Mangifera indica, Nicotiana tabacum* and *Rumex acetosella* were mentioned for their anti-proliferative and cancer growth retardation capabilities in texts from 1800 to 1945 (Supplemental file 3 – Traditional data extraction tables). The herbs were specified as a remedy or cure for cancer (6%), followed by herbs for their palliative, astringent, narcotic, sedative, antispasmodic and stimulant characteristics (15%). Several herb entries noted its use to improve physical wellbeing (32%), retard cancer growth (4%), control hemorrhage (14%), and manage cancer cachexia and diathesis (2.1%) (Fig. 4).

3.2. Herbal medicines from contemporary texts for lung and colorectal cancer

The contemporary naturopathic text search for the period from 1945 to 2022 yielded a total of 1233 citations from which only three studies with seven herb entries aligned with the inclusion criteria (Table 2). The two texts of Australian origin mention the use of herbs in the management of general and lung cancers only. *Curcuma longa* was included in two texts (n = 2) with specific mechanism of action to decrease risk of circulating tumor cells and provide nutritional supplementation. Other herbs included in the contemporary texts include *Calendula officinalis, Hydrastis canadensis, Echinacea purpurea,* medicinal mushrooms, *Astragulus membranaceus, Uncaria tomentose, Eleutherococcus senticosus, Panax ginseng, Withania somnifera, Rhodiola rosea, Centella asiatica, Cannabis sativa and Viscum album* (n = 15) [21,22]. These herbs assist with wound-healing, increasing immunity, rebuilding healthy body functions, retarding primary cancer growth or post-surgery support. *Viscum album* was administered in conjunction with chemotherapy and found to be effective in reducing chemotherapy-related toxicity [23]. The plant part used, preparation method of the herb, and dosages prescribed were not mentioned in the texts.

3.3. Herbal medicines from case studies for lung and colorectal cancer

From the 113 case studies identified, 10 case studies were eligible for inclusion: eight lung cancer and two colorectal case studies (n = 1, Duke's stage C adenocarcinoma and n = 1, rectal cancer). The types of lung cancer identified included non-small cell lung cancer (n = 2), small cell lung cancer (n = 1), malignant pleural mesothelioma (n = 1), adenosquamous cell carcinoma (n = 1) and adenocarcinomas (n = 1). Most studies included administration of herbal medicine alone (n = 6) or in conjunction with conventional chemotherapy (n = 4).

10 different herbal combinations published between 1800 and 2022 were identified from the case study search. Most case studies were from Korea (n = 3) and China (n = 3) while remaining originated from Taiwan (n = 2) and Japan (n = 1). Only one case study was noted from traditional texts written in the USA. These herbal preparations were of multiple herbs, and while plant parts used were not specified in all compositions, most included the use of root, bark, rhizome, pericarp, tuber, fruit, leaf and twigs, and cortex at different dosages. The preparations were prescribed in the form of decoctions (n = 3), aqueous extracts (n = 1), capsules (n = 1), preparations (n = 1) and four reports did not specify the administration type. (Table 3). The herbal treatment duration differed in range between six months to five years, and dosages were patient specific.

The case studies of Asian origin (n = 9), included use of traditional herbal medicine authentic to its country of origin, such as traditional Korean or Chinese medicine, and indicated no relevance to naturopathic practice. The case studies did not show repetitive use of the same herbal approach as each preparation and prescribed medication was specific and unique to the patient. The nine herbal treatment plans consisted of different combinations of 51 different herbal species with *Atractylodis* sp. (n = 5), Ginseng (n = 5), *Astragalus* sp. (n = 4), *Glycyrrhizae* sp. (n = 3), *Pinelliae* sp. (n = 3), *Poria* sp. (n = 3), *Scutellaria* sp. (n = 3), Solanum sp. (n = 3), *Angelicae* sp. (n = 2) and *Cinnamomum* sp. (n = 2) that commonly recurred (Table 3). Use of the traditional Chinese medicines (TCM), Hanshirento, zenshikunshito, and ninjin'yoeito caused negative patient outcomes and delayed the lung cancer patient for chemotherapy (n = 1). As the patient showed severe fatigue upon receiving this, the medicine was discontinued after two weeks and administered adjuvant chemotherapy at which the baseline laboratory tests indicated moderate liver injury that was attributed to the use of TCM [24].

One case study from traditional texts in 1908 included management of rectal cancer with *Thuja* sp., *Baptisia* sp., *Iris versicolor*, *Phytolacca* sp., *Echinacea* sp., *Gelsemium* sp., *Claviceps* sp., *Collinsonia* sp. and showed reduced tumor size. Interestingly, *Gelsemium* sp. and *Collinsonia* sp. were not mentioned in any other traditional texts.

4. Discussion

The current scoping review used both traditional and contemporary sources to identify herbal medicines and approaches to managing cancer. The traditional texts identified numerous herbal species used to treat cancer compared to case studies and contemporary naturopathic texts, but it is of note that current review only included contemporary texts in the context of colorectal and lung cancers while traditional texts examined all cancers. The most frequently mentioned herbs include

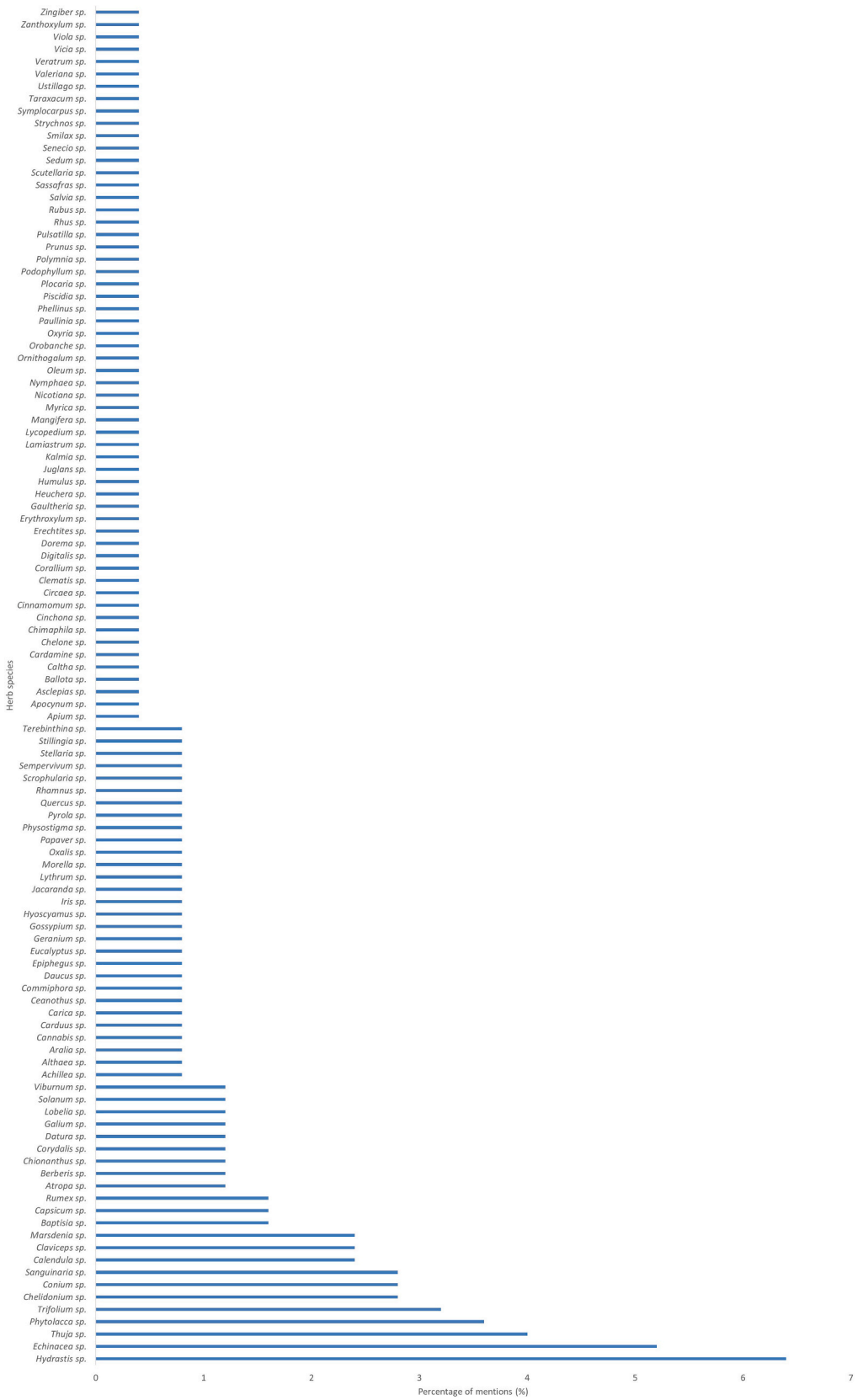

Fig. 2. Percentage mention of medicinal herbs used in traditional practice for cancer management
Values are expressed as percentage mention per herbal entry; n = 250 for total herb entries
Botanical names of five traditional herbs have recently changed: Corydalis sp./Corydalis formosa (New botanical name: Dicentra canadensis), Oleum sp./Oleum Betulae Empyreumaticum (New botanical name: Betula alba), Orobanche sp./Orobanche Virginiana (New botanical name: Epifagus virginiana), Plocaria sp./Plocaria helminthocorton (New botanical name: Fucus helminthocorton), Rhamnus sp. (New botanical name: Frangula californica). The table contains the traditional text name.

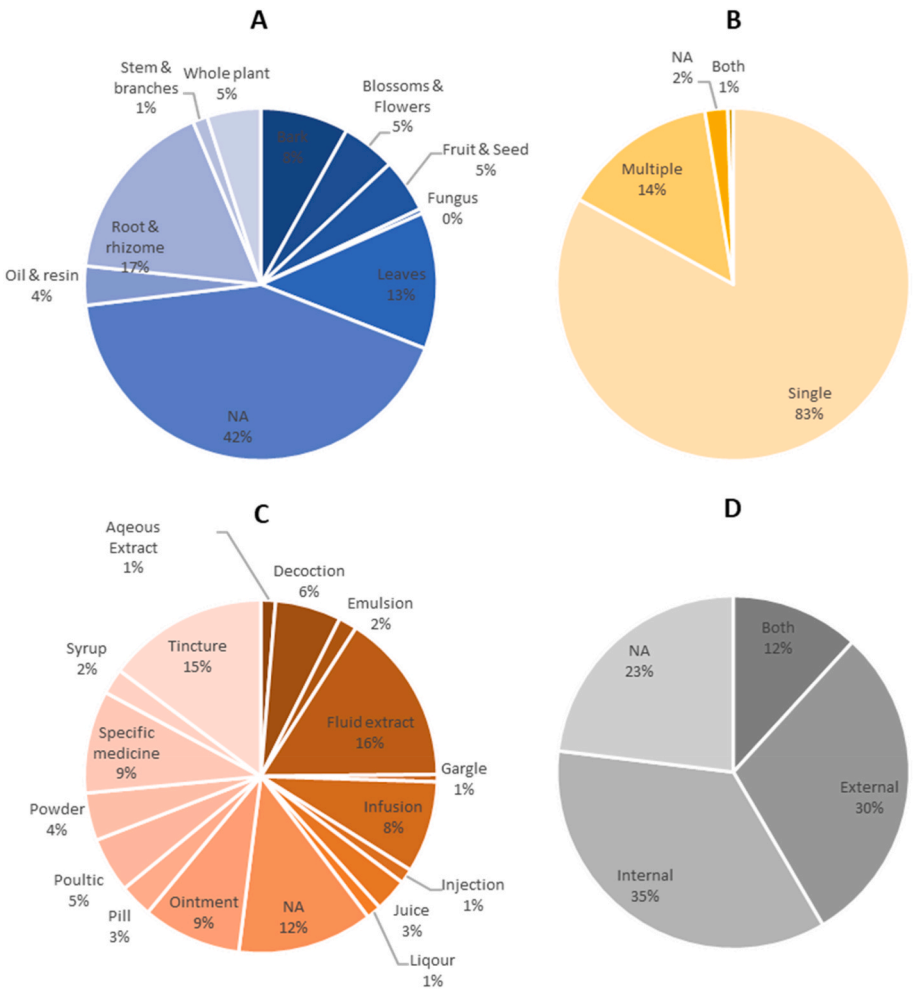

Fig. 3. Percentage mention of different A) plant parts, B) remedy type, C) preparation type, and D) administration method of medicinal herbs used in traditional practice for cancer management

1 Values are expressed as percentage mention of plant part/remedy type/preparation type/administration method from total entries; total (n = 222 for plant part, n = 194 for remedy type, n = 297 for preparation type, n = 194 for administration method). NA: Not Available

2 Juice was obtained from grinding the specific part of the herb, herbal liqueurs were spiced with herbs and were considered sweetened spirits, infusion involved steeping the herb in a liquid (generally water) and tinctures were concentrated herbal extracts made by soaking the specific plant part/s in alcohol or vinegar.

Hydrastis canadensis, *Echinacea angustifolia* and *Thuja occidentalis* (traditional texts), *Curcuma longa* (contemporary texts) and *Atractylodis* sp., Ginseng and *Astragalus* sp. (case studies). Reasons for utilising herbal medicines was diverse across traditional, contemporary naturopathic practice and individual case management and included retardation of cancer growth, anti-carcinogenic activity, cancer prevention, hemorrhage control and overall curative effect. Interestingly, while traditional and contemporary approaches mostly included single-herb preparations, the case studies noted in this review administered compounded herbal prescriptions with multiple ingredients as they were predominantly from East Asia (Table 3) based on the philosophy of "principal-assistant-adjuvant-mediating guide" to achieve comprehensive therapeutic efficiency [35].

Retardation of cancer growth was a common phenotype noted across traditional and contemporary clinical practice with increased awareness of toxicity of herbs. Herbs such as *Hydrastis canadensis*, *Conium maculatum, Claviceps purpurea, Echinacea* sp. *Carica papaya, Chelone glabra, Corallium rubrum, Daucus carota, Epifagus virginiana, Lamiastrum galeobolon, Mangifera indica, Nicotiana tabacum and Rumex acetosella* (traditional texts), *Cannabis sativa* (contemporary) and *Antrodia cinnamomea* and compound prescriptions of Chinese herbal medicines (case studies) were all identified to be administered specifically to retard cancer growth. While anti-carcinogenic activity of some of these listed herbs has been supported by pre-clinical studies with use of immortalized cancer cell lines [36–44], it is important to note that traditional and contemporary clinical use may not be aligned due to incorrect botanical identification or discovery of the herbs' toxicity, thereby altering the preparation and dosage of these herbal extracts over time. For example, traditional evidence shows that *Conium maculatum* (poison hemlock) 'retards distress in glandular enlargements in scrofulous or cancerous cachexia' [19] in doses of two to six minims of its fluid extract, but it is a well-known as a highly poisonous and deadly herb when ingested due to its toxic alkaloids affecting nerve impulse transmission to muscles causing respiratory failure [45]. Yet, *Conium maculatum* is still used in current homeopathic clinical practice to treat the cancer specifically as an 'organ remedy' in very low potencies for different cancers [46], and pre-clinical research supports the preferential cytotoxic effects in breast cancer cell lines [3,3,47](Frenkel et al., 2010)(Frenkel et al., 2010). It is imperative to note that *Conium maculatum* is also mistaken with *Daucus carota* (wild carrot) [48] used to 'degenerate malignant ulcers and abscesses' [49] but *Daucus carota* is not highly toxic when ingested. This mistaken identity of a possibly deadly plant is due to the close resemblance of the two plants as they both belong to the same Umbellifers family. This suggests that even though herbs have similar specific cancer outcomes (e.g. cancer growth retardation) across traditional and clinical practice, the incorrect identification, dosage or preparation method of

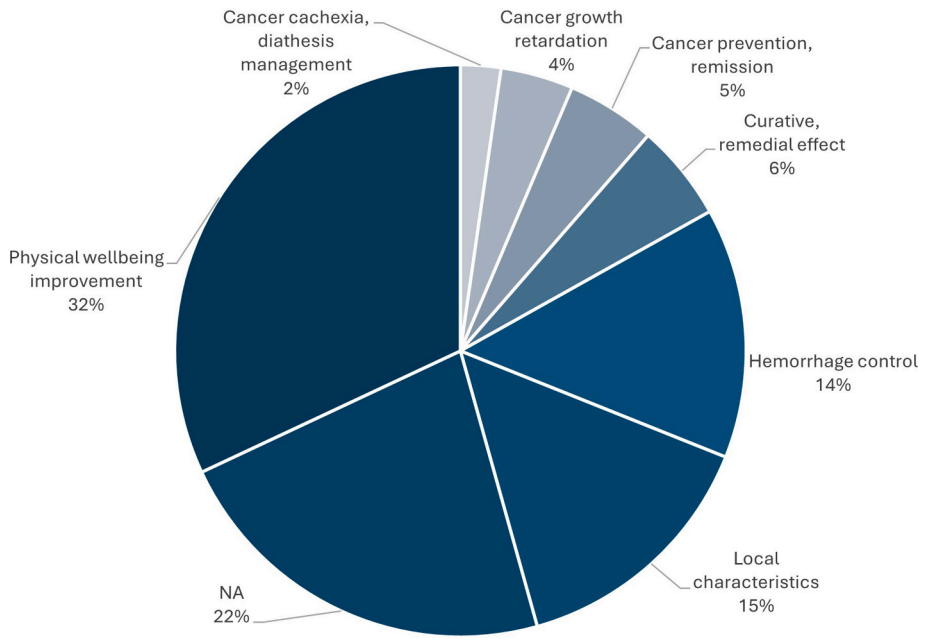

Fig. 4. Percentage mention of mode of action for medicinal herbs used in traditional practice for cancer management
Values are expressed as percentage mention of plant part/remedy type/preparation type/administration method from total entries; total (n = 223 for plant part, n = 195 for remedy type, n = 298 for preparation type, n = 195 for administration method). NA: Not Available
Cancer growth retardation refers to specific mention of 'retards cancer growth, controls growth, prevents engorgement' and curative or remedial effect refers to 'reputed remedy, cure for cancer, or dissolving of tumor'.

Table 2
Medicinal herbs used for treatment of cancer and their outcomes in contemporary practice

No	Citation	Cancer of Interest	Herbal medicine (Latin Name)	Herbal medicine (Common names)	Treatment plan/ Administration	Purpose
1	[21]	General	*Curcuma longa and Ginkgo biloba*	Turmeric and gingko	Internal	• nutrient supplementation with fish oils, vitamin E, **turmeric** and herbs such as **ginkgo** that could increase the risk of bleeding should be stopped before 1 week of general surgery
2	[22]	General	*Calendula officinalis, Hydrastis canadensis*	Common marigold, golden seal	NA	• wound healing herbs • Post-surgery support for tumour removal
3	[22]	General	*Echinacea purpurea, Uncaria tomentose, Astragulus membranaceus, medicinal mushrooms*	Purple coneflower, Cat's claw, Astragalus, medicinal mushrooms	NA	• Increase immune function/system • Post-surgery support for tumour removal
4	[22]	General	*Uncaria tomentose, Curcuma longa*	Cat's claw, turmeric	NA	• Reduce any risk of circulating tumour cells • Post-surgery support for tumour removal
5	[22]	General	*Eleutherococcus senticosus, Panax ginseng, Ashwagandha, Rhodiola rosea, Centella Asiatica*	Siberian ginseng, true ginseng, winter cherry, Rhodiola, Gotukola,	NA	• Rebuild the body to a healthy state prior to the start of further cancer treatment • Adaptogenic herbal medicine • Post-surgery support for tumour removal
6	[22]	Lewis lung adenocarcinoma and general	*Cannabis sativa*	Hemp	NA	• Reduce the primary cancer growth (The cannabinoids delta-9-THC, delta 8-THC and cannabinol but not CBD) • cannabinoids can limit inflammation, cell proliferation and cell survival (via CB1 and CB2 receptors - *in vitro*)
7	[23]	General	*Viscum album*	Iscador or Mistletoe	• Chemotherapy alone or chemotherapy plus iscador thrice weekly until tumour progression. • Chemotherapy consisted of 21-day cycles of carboplatin combined with gemcitabine or pemetrexed.	• safe and effective adjunctive treatment for cancer that assists in reducing chemotherapy-related toxicity

* Specific references related to No 2, 3, 4, 5 and 6 can be found in the indicated reference.

the herb may not align with traditional practice and could be fatal.

Analysis of traditional and contemporary sources showed a clear loss of herbal knowledge transfer from traditional to contemporary practice. *Calendula officinalis, Hydrastis canadensis, Echinacea* sp. and *Cannabis sativa* are the only herbs identified in contemporary clinical practice from 110 traditional herbs. While this current review focused only on

Table 3
Medicinal herbs used for treatment of cancer, their preparation type, administration method and associated outcomes in individual case management Fig. 4: List of Herbal Species Mentioned in Different Herbal Preparations in Case Studies

No	Citation	Country	Cancer of interest	Treatment Plan	Composition of herbal medicine	Preparation Type/plant part and dosage	Administration Method/duration	Single or mixed?	Outcome
1	[25]	Korea	advanced non-small-cell lung cancer (NSCLC)	gefitinib (250 mg/d) and traditional herbal medicine, modified Bojungikki-tang	Ginseng radix, Astragali radix, Liriopes radix, Magnoliae obovatae cortex, Zingiberis rhizoma recens, Atractylodis japonicae rhizome, Angelicae gigantis radix, Citri reticulati exocarpium et mesocarpium, Glycyrrhizae uralensis radix et rhizome, Pinelliae tuber, Zizyphi fructus, Cervi Pantotrichum Cornu, Agastachis Herba, Perilla Folium	Not specified/ as in [25]	Internal/1 year (3 times per day, 30 min after every meal based on symptoms)	Mixed	• Partial response achieved, but severe papulopustular skin rashes developed and aggravated after 3 months. • Gefitinib dose was reduced and PFS maintained for approximately 78months
2	[26]	Japan	Lung cancer	Traditional chinese medicine post-surgery, hanshirento, zenshikunshito, and ninjin'yoeito	**Hanshirento**: Scutellaria barbata, Elfvingia, Oldenlandia diffusa, Glycyrrhizae Radix, Semen Coicis **Zenshikunshito:** Ginseng Radix, Magnoliae Cortex, Perillae Fructus, Citri Unshiu Pericarpium, Poria, Angelicae Acutilobae Radix, Atractylodis Rhizoma, Amomi Semen, Saussureae Radix, Aquilariae Lignum, Mori Cortex **Ninjin'yoeito:** Rehmannia Radix, Astragali radix, Ginseng Radix, Cinnamomi Cortex, Polygalae radix, Paeoniae radix, Schisandrae Fructus **Sairei-to:** Bupleuri radix, Alismatis Tuber, Pinelliae Tuber, Scutellariae Radix, Atractylodes lancea rhizome, Ziziphi Fructus, Polyporus sclerotium, Ginseng Radix, Poria Sclerotium, Glycyrrhizae Radix, Cinnamomi Cortex, Zingiberis Rhizoma	Not specified/ as in [26]	Internal/2 weeks	Mixed	• Induced repeated moderate liver injury • Induced fatigue • delayed for chemotherapy
3	[27]	Korea	malignant pleural mesothelioma (MPM)	Korean herbal medicine, Gunchil-dan and Bangam-tang	**Gunchil-dan:** *Rhus verniciflua* Stokes (RVS) **Bangam-tang**: *Astragalus membranaceus* Bunge, *Atractylodes macrocephala* Koidzumi, *Poria cocos* Wolf, *Pinellia ternata* Breitenbach, *Citrus unshiu* Markovich, *Agastache rugosa* O. Kuntze, *Alisma orientale* Juzepczuk, *Plantago asiatica* Linné, *Spatholobus suberectus* Dunn, *Zizyphus jujuba* Miller var. inermis Rehder, *Glycine* max	Capsule/as in [27]	Internal/21 months (twice-daily Gunchil-dan and thrice-daily Bangam-tang)	Mixed	• no significant interval changes and progression • no significant adverse events occurred

(*continued on next page*)

Table 3 (*continued*)

No	Citation	Country	Cancer of interest	Treatment Plan	Composition of herbal medicine	Preparation Type/plant part and dosage	Administration Method/duration	Single or mixed?	Outcome
					Merrill, *Crataegus pinnatifida* Bunge, *Hordeum vulgare* Linné var. hexastichon Aschers, *Prunus mume* Siebold et Zuccarini, and *Glycyrrhiza uralensis* Fischer.				
4	[28]	Korea	Small cell lung cancer (SCLC)	dish-cultured *Antrodia Cinnamomea (DAC)*	DAC with an increasing dosage, from 5 g/d up to 10 g/d DAC, for six months, without radiation or chemotherapy treatment	dissolved in water/5–10 g/d DAC, for six months	Internal/6 months	Single	• tumor shrunk substantially • patient survived for 32 months without relapse after 6 treatment.
5	[29]	Taiwan	adenosquamous cell carcinoma of the lung	Botulinum toxin *type A (onabotulinumtoxin A)*	Botulinum toxin *type A (onabotulinumtoxin A)*	Not specified	Internal/1.5 years (Injection)	Single	• improvement in facial flushing and pain • No adverse effects or complications were noted during the subsequent 1.5-year therapeutic course.
6	[30]	Korea	stage IV adenocarcinoma of lung	gefitinib (250 mg/d) and complementary herbal medicines	Ginseng, Fomes fomentarius, Inonotus obliquus, Phellinus linteus	Not specified	Internal/9 weeks	Mixed	• clinically relevant interaction of gefitinib with complementary herbal medicines. • complementary herbal medicines causing treatment failure in a patient who was subsequently responsive to gefitinib.
7	[31]	China	Stage IV lung cancer	Chinese herbal medicines and Chinese patent medicines	**Strengthening herbs:** Codonopsis pilosula, Astragalus membranaceus (Fisch.) Bge, Rhizoma Atractylodis, Poria cocos, Tangerine Peel, Pinellia ternate, Semen Armeniacae Amarum, Rhizoma rehmanniae, Folium mori **Detoxification herbs:** Solanum lyratum, Solanum nigrum, Sculellaria barbata, Salvia chinensis, Prunella vulgaris, Indian Iphigenia Bulb, Radix Ranunculi Ternati, Hedyotis diffusa, Herba Taraxaci	Decoction/as in [31]	Internal/5 years, 1 month (150 mL each time, twice a day, 1 h after breakfast and dinner)	Mixed	• improved quality of life (including improvement of symptoms and performance status score) • prolonged survival • delayed speed of tumor progression because of the CM treatment
8	[32]	China	NSCLC	Gefitinib and Chinese herbal medicine, "Fuzheng Kangai''(FZKA)	**Fuzheng Kan- gai**: Pseudostellaria hetero-phylla (Miq.) Pax ex Pax et Hoffm. (Taizishen), Atractylodes macrocephala Koidz, Astragalus membranaceus (Fisch.) Bge, Oldenlandia diffusa (Willd.) Roxb, Solanum nigrum L. , Salvia chinensis Benth, Cremastra appendiculata (D. Don) Makino, Coix lachrymal-jobi L, Akebia	Decoction/as in [32]	Internal/5 years, 5 months (2 equal portions and taken warm, twice a day)	Mixed	• Suggested CHM (FZKA) may have a synergistic effect on gefitinib

(*continued on next page*)

Table 3 (*continued*)

No	Citation	Country	Cancer of interest	Treatment Plan	Composition of herbal medicine	Preparation Type/plant part and dosage	Administration Method/duration	Single or mixed?	Outcome
					quinata (Thunb.) Decne, Rubus parviflolius				
9	[33]	China	Duke's stage C adenocarcinoma	integrative treatment and herbal medicine Huai Hua Di Yu Tang and Bai Tou Weng Tang	Sophora Japonica, Pulsatilla sp.	Pagoda Tree Flower and Sanguisorba Root Decoction and Pulsatilla Decoction	Internal/2 years	Mixed	Integrative treatment managed chemotherapy side effects
10	[34]	USA	Rectal	Herbal medicine only	Thuja sp., Baptisia sp., Iris versicolor, Phytolacca sp., Echinacea sp, Gelsemium sp, Claviceps sp., Collinsonia sp.	Preparation of Thuja	Internal (Thuja – injection)/not specified	Mixed	•control circulation of the rectum • tumor had been reduced to about the size of a cherry from the size of a quail egg in 4 months

colorectal and lung cancers in contemporary literature, it is important to note that *cancer* in traditional knowledge was not defined in the same way as it is today. While this loss of knowledge from traditional to contemporary practice needs to be more closely examined, it may be explained by historical movement of cultures, mixing of herbal use knowledge and increased technology advances. History clearly shows movement of cultures and mixing of herbal use – e.g. traditional practice known as a physio-medical or Anglo-American system associated a style and practice of herbalism that merged American, England and European herbs. This traditional practice was eclectic, blending herbal medicine with medical approaches [50], as seen in the traditional texts that show use of different diets, use of metals and acids, and gun powder along with surgery in cancer treatment in conjunction to herbal medicines [19,51,52]. In 1970s, social and political changes occurred in the USA with the start of the Vietnam war [50] and this change saw an emergence of counter cultures of different lifestyles and philosophies, herbal renaissance and rise in objections to conventional medicine on a global scale. In Australia, a move from Anglo-American based herbal medicine system to a mixed medicine system introduction of herbs from other native medical systems, such as Gingko, Dong Quai (TCM), Billbery and turmeric, or countries, including *Withania somnifera* from India, *Uncaria tormentosa* from South America and *Rehmannia glutinosa* from China, into Materia Medica of Australian western herbalists [53] and into contemporary lung cancer management (Tables 2 and 3) [50].

While traditional practice showed eclectic use of herbs, technological and methodological advances have been driving the reductionist approach to herbal use - these advances increased our understanding of potential anti-cancerous active ingredients, but also resulted in a profound shift in use of herbs and herbal preparations. For example, *Hydrastis canadensis* (Goldenseal) frequently mentioned in traditional texts examined in this review, was administered as a strong decoction, or infusion (Supplemental file 3 - Tables 1–3, 5 and 6). However, in contemporary practice it is extracted with 60% ethanol to ensure highest extraction of the representative alkaloids, regardless of any other possible active ingredients that may be present in aqueous solutions [50,54]. Further, while traditional knowledge indicates herbs such as *Calendula officinalis* can be administered as an infusion, extract, tincture or topical application, the laboratory studies only examined cream preparations for prevention and treatment of radiation-induced skin toxicity with mixed results [55,56].

The shift of herbal use between tradition and contemporary practice also saw introduction of legislative limitations – e.g. traditional medicinal herbs such as *Lobelia inflata*, *Gelsemium* sp., *Atropa belladonna*, *Datura* sp., *Digitalis* sp., *Hyoscyamus niger* were used for treatment of stomach and bowel, rectal, liver, mammary, general and digestive cancers, respectively. All of these herbs are currently scheduled or restricted in Australian contemporary practice due to their inclusion in Standard for Uniform Scheduling of Drugs and Poisons by Therapeutic Goods Administration (TGA) [57]. Much like *Conium maculatum*, *Gelsemium* sp. was restricted as it causes respiratory depression when used in high doses - it is of note that this use is not aligned to traditional practice (Table 3) [58,59]. On the other hand, while contemporary research may be limiting the use of some herbs, for others it is a necessary precaution to use as herbal preparations, as is the case for *Digitalis* sp. - traditional knowledge acknowledges possible anti-cancer properties, contemporary research also shows its therapeutic use in heart conditions but only under strict consumption guidelines as excessive use of the active ingredient group of glycosides can lead to death due to cardiac arrest [60,61]. Therefore, contemporary research can assist in understanding herbal medicines at the level of biologically active phytochemistry.

In an attempt to develop new anti-cancer pharmacological approaches, herbs from traditional and contemporary practice have been widely researched using *in vitro* models. For example, the English extract and specific conium made of full-grown *Conium maculatum* fruit and leaves was traditionally used for mammary cancer (Supplemental file 3-Table 5) and has shown to reduce viability and proliferation of HeLa, a cervix carcinoma cell line when administered as an ethanolic extract [62], indicating research of traditional herbs in different parts of the body apart from its traditional use. Similarly, fluid extracts and specific medicines of *Claviceps purpurea* were used in uterine cancers (Supplemental file 3 – Tables 1 and 2) and, in line with its traditional use, alkaloids of *Claviceps purpurea* have been found to exert cytotoxicity effects in a multi-factorial manner in colon, lung, CNS, kidney, prostate, ovarian, breast, melanoma, and leukemia cancer cell lines in Ref. [63]. Further, pre-clinical studies have identified an alkaloid (Sanguinarine) present in the root of *Sanguinaria canadensis* which has shown to facilitate ferroptosis in growth and spread of NSCLC *in vitro* if isolated [64].

Interestingly, this review also identified that certain herbs were repurposed from traditional to contemporary practice and pre-clinical research across cancer types. For example, while *Scutellaria* sp. is used in traditional and complementary medicine as a standalone herb for unspecified cancers (Supplemental file 3 – Table 1) [4], in contemporary case studies we show use of its root for mixed preparations for lung cancer (Table 3). This finding is in line with current pre-clinical literature that indicates that an ethanol extract of dried root of *Scutellaria baicalensis* inactivates STAT3 pathway in lung cancer cells and induces apoptosis [65], but also extends its use to other cancer types – e.g. its natural active ingredients, baicalein and baicalin from roots [66] also inhibit colon cancer through apoptosis and senescence [67]. This

suggests that a greater overlap of the herbal preparation knowledge provided by traditional medicine and modern research methodologies could potentially discover new plant-based or derived substances with low intrinsic toxicity to normal cells but deleterious effects on cancerous cells and provide insights to repurposing herbs across different cancer types.

Overall, this current scoping review clearly shows importance of interplay between tradition, contemporary clinical practice and research in a way that is beneficial and effective for human health. This interplay is an important point to consider for understanding implementation of tradition into contemporary contexts, from clinical practice to legislation, for understanding herbal mode of action and discovery of new cancer treatments.

5. Limitations

The searches only included texts and studies written and published in English or could be translated to English and accessible through online resources that may have missed relevant publications on other native and indigenous herbal medicines. The literature search for traditional medicine was limited to 1800 to 1945, however this search found relevant traditional texts from 1700s, that needed to be excluded due to the inclusion criteria. Due to accessibility of the literature, search identified very limited Ayurveda herbs (tumeric, Ashwagandha and gotu kola).

6. Conclusion

In conclusion, this scoping review provides an insight to what has been documented from traditional and contemporary texts and literature examining the potential anti-cancer activity of herbal medicine world-wide. Only *Hydrastis canadensis, Calendula officinalis, Echinacea* sp. and *Cannabis sativa* are the commonly prescribed herbs with retarding cancer growth outcome across the traditional and contemporary data sets. Different historical and cultural influences resulted in this loss of knowledge transfer. It is imperative to note that these some of these traditional and contemporary herbs and their active ingredients have been studied in *in vitro* models and the data extracted in this review, can be considered in pre-clinical and clinical research.

Authors contribution

Conceptualisation, Project Administration: AB; Methodology: IR, JS, AB; Formal analysis, Investigation, Data Curation, Visualisation, Writing – Original IR; Validation, Writing – Review & Editing, Supervision JS, AB.

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Appendix A. Supplementary data

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