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Review Article

# Integrating ayurvedic medicine into cancer research programs part 2: Ayurvedic herbs and research opportunities

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ABSTRACT

The aim of this two-part review in this issue is to provide some basic perspectives from Ayurveda, the traditional medicine of India, and to discuss how current research methodologies may be used to shed light on mechanisms of Ayurvedic treatments to support cancer care and prevention. It addresses some of the challenges for scientific validation of Ayurvedic herbal compounds, protocols, and modalities in four areas. Part 1 [1] has reviewed Ayurvedic theories and applications of body constitution (*Prakriti*), digestion (*Agni* and *Ama*) and mind-body-spirit health in relation to cancer. Here in Part 2, the focus is on preclinical and clinical research of Ayurvedic botanical herbs, with a review of pertinent literature on three selected herbs, Curcumin, Ashwagandha, and Triphala. A discussion of the challenges and possibilities of research in Ayurveda is offered to guide the development of translational research programs. Ayurvedic modalities are not intended as a substitute for allopathic treatments of cancer but as an integrative component for prevention and restoration of strength and immunity.


## 1. Introduction

While Ayurveda includes many modalities and approaches to health, the published research in Ayurveda is largely represented by studies of the herbs and botanical formulas. There are hundreds of Ayurvedic herbs described in Ayurvedic texts and used throughout millennia for prescribed medicinal uses. Traditional recipes of these herb mixtures are called "*Rasayanas*" which are formulas of herbs, used in preventive and regenerative medicine, particularly for increasing strength and immunity and reversing the ageing process. Ayurvedic herbs (*Dravya*) are grouped according to their main effects on imbalances in the *doshas(Vata, Pitta and Kapha) (see Part 1 of Review* [1]*)* and *dhatu* (tissues), providing corrective qualities ("*gunas*") for the patients according to the principle of *Dravyaguna* [2]. These formulations may also target numerous biochemical pathways possessing a potential synergy of effects to nourish the body as a whole by supporting various organ systems [3]. A comprehensive survey from 2001 by The New York Botanical Gardens reported pre-clinical and clinical studies of 166 Ayurvedic herb species. These studies were mostly preliminary studies from the 1990s but may help to direct research on plants deserving of more intensive evaluation as clinical therapies [4].

Another extensive compilation of the herbal monographs and formulations is presented in The Ayurvedic Pharmacopoeia of India as an official document of the AYUSH ministry of the Government of India. These are multiple volumes of monographs of various herbs with analysis and quality standards for safety and efficacy [5]. Also see the database "Traditional Knowledge Digital Library (TKDL) [6] for a list of medicinal plants and formulations from the texts of traditional medicine systems of India including Ayurveda, Unani, and Siddha. This site also addresses the need for maintaining the intellectual property rights for the traditional knowledge of Ayurveda [7].

According to classic Ayurvedic texts, *Rasayana* therapy can slow the aging process and enhance immunity, intelligence, memory, strength, youth, luster, and vitality. These herbs are purported to nourish the tissues of lymph, blood, muscle, adipose tissue, bone, nervous and reproductive systems, prevent degeneration and illness, and have been effective as radioprotective and chemoprotective agents [8]. Many of the herbs have been evaluated for their use in the mitigating side effects of cancers treatments and enhancing immunity - See Table 1.

Much of the literature on Ayurvedic herbs available is preclinical and relates to defining mechanisms of the individual chemical

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**Table 1**
Anticancer mechanisms of common ayurvedic herbs.

| HERB | References and mechanisms addressed |
|---|---|
| Curcumin/turmeric (*Curcuma longa*) | • Reviews details of modulation of pathways of cell proliferation, cell survival, caspase activation, tumor suppressor, death receptor, protein kinase, and mitochondrial pathways [57],<br>• Reviews the role in the protection of cancer as well as neurological, cardiovascular, and gastrointestinal diseases mainly through anti-inflammatory and antioxidant action. Also addresses antiviral and antiparasitic potency of curcumin (in vitro and in vivo) [13]<br>• Role in prevention of cancer progression [58]. |
| Guduchi/Amrut (*Tinospora cordifolia*), | • Has radioprotective role and is a strong free radical scavenger, anti-cancer effects, immunomodulatory, anti-diabetes property, anti-toxic effects, anti-arthritic, anti-osteoporotic effects [59] |
| Pippali (*Piper longum*), | • Piperine is an alkaloid from black pepper that can inhibit human colon cancer cell growth by G1 arrest and endoplasmic reticulum stress induced apoptosis [60] |
| Triphala: Haritaki (*Terminalia chebula*),<br>Bibhitaki (*Terminalia bellirica*),<br>Amalaki (*Emblica officinalis*) | • Triphala, as a novel anticancer drug [31]<br>• Reviews formulation for treating and preventing cancer: [28].<br>• Antioxidant activity [61]<br>• Inhibiting Angiogenesis [30] |
| *RASAYANAS*<br>Ashwagandha *(Withania somnifera*), Guduchi *(Tinospora cordifolia*), and Shatavari *(Asparagus racemosus*)<br>Ayurvedic *Rasayanas* [15] reviewed | • Herbal combinations provided immunoprotection and myeloprotection during cancer chemotherapy with cyclophosphamide (CP)-in mice with ascitic sarcoma without compromising CP anti-tumor activity [62]<br>• A review of 15 *Rasayana* herbs with antioxidant properties that work across organ systems and diseases including anti-aging, cancer, diabetes, inflammation, etc [63] |
| Multiple *Rasayanas Withania somnifer*a, Brahma *Rasayana* (BR), (36 herbs)<br>*Rasayanas* – Maharishi Amrit Kalash- 4 (MAK-4) and MAK-5 | • Provide Adjuvant therapy to Radiation and Chemotherapy treatments for cancer. Protection of normal tissues [8,29,64,65].<br>• Inhibit LDL oxidation in hyperlipidemic patients. Reduce severity of atherosclerosis [66,67] |
| Ashwagandha, Withaferin A<br>*Withania somnifera (Linn Dunal*) | • Anticancer mechanisms of Withaferin A in glioblastoma (GBM) [68].<br>• Anticancer Mechanisms of Withaferin A in Breast Cancer [69]<br>• Toxicity, pharmacokinetics and pharmacodynamics, immuno-modulating properties [70]<br>• Anti-microbial, anti-stress, neuroprotective, cardioprotective, and anti-diabetic properties [70]<br>• Withanolides used clinically in inflammation-mediated chronic diseases (including arthritis, autoimmune, cancer, neurodegenerative, and neurobehavioral). Pathways involved include NF-κB, JAK/STAT, AP-1, PPARγ, Hsp90 Nrf2, and HIF-1 [71].<br>• Withaferin-A suppresses experimentally induced carcinogenesis, via anti-oxidative, anti-inflammatory, anti-proliferative and apoptosis-inducing properties [72].<br>• Cancer prevention and treatment (good reviews) [9,73]<br>• Preventive and anticancer effect of Withaferin A include molecular targets and mechanisms [22]. |

components for drug discovery. But this current 'one target-one drug (or herb)' approach is limited. The body develops resistance to many drugs. Combinations of drugs are needed to act on several targets simultaneously. Most of the diseases have multi factorial causation and multiple molecular targets. Traditional formulations such as in Ayurveda are multi-component and have centuries of clinical application. There may be an inherent value of these complex formulations for complex diseases. Unique mechanisms of action may be found in exploring these botanicals.

How do we decipher the synergy of these herbs in combinations? Herein is the research dilemma with Ayurveda. We need a more whole systems approach to understand the combined effects of these compounds.

## 2. Mechanistic and clinical studies in ayurvedic herbs

This review will briefly highlight three of the most promising and commonly researched Ayurveda herbs or formulas related to their efficacy for cancer: Curcumin, Ashwagandha, and Triphala. Curcumin is the most researched single compound from the Ayurveda tradition and is accepted as valuable for its anti-inflammatory properties; Ashwagandha has been studied preclinically and clinically and found to have multiple anti-cancer properties [9]; while Triphala is a combination of herbs used as a tonic for the bowel and has anticancer properties and radioprotective and chemoprotective effects.

### 2.1. Turmeric: curcumin (Curcuma longa)

Turmeric (*C. longa*) is a member of the ginger family (Zingiberaceae) and is used extensively in foods and in Ayurvedic and Chinese systems of medicine. In Ayurveda, it was traditionally used for disorders of the digestive system, skin, joints, and upper respiratory tract. Curcumin is a lipophilic flavonoid extracted from *C. longa*. Numerous preclinical and clinical trials have validated its role in a variety of human chronic diseases: inflammation, metabolic disorders, neurological, cardiovascular, infectious, skin diseases, and cancer [10,11]. PubMed posts 19,831 references on "curcumin" with 7066 results for "curcumin and cancer" (August 2022). One review focuses on curcumin's targeting of PI3K/AKT to inhibit cancer development and progression in different malignancies [12]. A review by Liczbinski et al. [13], outlines the numerous effects of curcumin for cancer as well as neurological, cardiovascular, and gastrointestinal diseases. In this reference, multiple anti-cancer mechanisms are discussed including effects of curcumin on apoptosis, reducing oxidative stress, cell cycle arrest in G2/M phase, modulating the proteasome, NF-KB, and cytokine activities, and regulating inflammatory responses. Turmeric and curcumin are challenging to study because curcumin is unstable and has low bioavailability when it is taken in tablet form. Also, curcumin products in the market may differ in composition which makes the results of research on these products difficult to understand and compare. Medicinal chemistry considerations of curcumin are included in a review by Nelson et al., 2017 [14].

While curcumin comes from the Ayurvedic tradition, the research to understand this isolated compound's specific mechanisms and efficacy does not always qualify as research in 'Ayurveda'. In Ayurvedic pharmacology, turmeric would likely be combined with other herbs such as piperine in black pepper for increased absorption, potency, and synergy [15]. Curcumin has also been found to interfere with the cytochrome P450 pathway and may counteract metabolism of some chemotherapeutic drugs if taken simultaneously [16].

#### 2.1.1. Clinical studies of curcumin

Some of the clinical research in curcumin includes studies in inflammatory diseases and in cancer. Clinicaltrials. gov reports 75 trials in curcumin for cancer prevention or treatment. Clinicaltrials. gov also lists 292 total studies (2022) with curcumin adding conditions not related to cancer, such as coronary artery disease, cognitive function, pain, gut microbiome, diabetes, chronic kidney disease and others. Many clinical studies may have small sample sizes and short duration [17] with difficulty in absorption [14] and higher doses resulting abdominal complaints [18]. A recent review of curcumin suggested that while there may be benefits for modulating side effects of chemotherapy, and synergy with the anti-cancer drugs, there is still a need for more robust clinical trials to employ curcumin as a part of anti-cancer treatments [19].

### 2.2. Ashwagandha (Withania somnifera)

Ashwagandha, also known as "Winter cherry" and "Indian ginseng," is one of the most valuable herbs in Ayurveda and is also well represented in the research literature. The phytochemical constituents include Withanolides and Withaferin A (WA; C-28 steroidal lactone triterpenoids) alkaloids, flavonoids, and other biologically active compounds. It is used traditionally as a rejuvenating herb that helps the body adapt to various types of stress (adaptogen); it also promotes stamina and general well-being [20]. The anticancer mechanisms of Ashwagandha or its metabolites, WA, were evaluated as therapeutic adjuvants for cancer [9]. This paper presented the varied mechanisms of ashwagandha in the context of the "hallmarks of cancer" which are reproducible cellular pathways that enable tumor growth and metastatic dissemination, as described by Hanahan and Weinberg [21]. These mechanisms include the production of reactive oxygen species (ROS) and inducing apoptosis in many types of cancer cells [22]. Research into mechanisms of Ashwagandha include blocking proliferation, reactivation of tumor suppressor genes, inhibiting angiogenesis, retarding metastatic progression, stabilizing the genome, anti-inflammatory and improving cancer immunosurveillance (See Table 1 for mechanisms and references).

#### 2.2.1. Clinical studies of ashwagandha

While Ashwagandha is one of the most studied herbs in Ayurveda, the clinical evidence for cancer prevention or therapy is yet to be determined. The few clinical studies of Ashwagandha reported in Clinicaltrials.gov relate mostly to cognitive or mental function, stress and anxiety, immune cell activation. Some studies are often inconclusive due to short trial duration, small sample size or confounding variables [23,24]. Important steps are needed for the clinical development of Ashwagandha such as long-term toxicology evaluation to establish safety, pharmacodynamics, and determination of biomarkers predictive of Withaferin-A tissue exposure.

### 2.3. Triphala

Triphala ("three fruits") is a valuable herbal Ayurvedic preparation and combines Amalaki or Indian Gooseberry (*Emblica officinalis*), Bibhitaki (*Terminalia bellirica*), and Haritaki (*Terminalia chebula*). Triphala is a powerful tonic for cleaning, toning, and rejuvenating the digestive tract; it detoxifies the liver, intestines and blood and promotes urinary tract health [25,26]. Triphala was shown to have a prebiotic effect to modulate gut microbiota in a study of in vitro anaerobic human fecal cultures. Triphala had profound changes in the relative abundance of many phylogenetically diverse gut species including a significant increase in butyrate-producing bacteria [27]. Triphala was discussed in Part 1 of this review in relation to the importance of optimizing digestion for supporting for maximum health. Triphala is rich in antioxidants, improves immunity, prevents degeneration and aging, and nourishes tissues [28]. Many preclinical studies have shown that Triphala is useful in the prevention of cancer and possesses antineoplastic, radioprotective and chemoprotective effects [28,29]. Triphala can target multiple diverse physiological processes, leading to a synergy of effects in the target cells as well as tissue microenvironment, immune system, and angiogenesis [30].

Existing preclinical models are not able to reproduce the full mechanisms of action or potential of these herbs. Often a compound is deemed effective based on cytotoxic or apoptotic effects for tumor cells in culture or *in vivo* tumors [31]. One approach to understanding potential of Ayurvedic pharma is through "Network Pharmacology". This concept was first described in 2007 and 2008 [32,33]. It extends beyond the assumption that there is one drug for one target for one disease. It proposes that many drugs may act on multiple targets rather than a single intended target. This concept has been advanced in exploring relationships between drugs, genes and diseases in Traditional Chinese Medicine [34].

Network pharmacology was the approach used by Chandan and Patwardhan to illustrate and decipher the complexity of Ayurvedic traditional herbs or formulas including Triphala [35] and Ashwagandha [36]. Network pharmacology integrates systems biology, -omics technologies and computational biology to study multi-component and multi-targeted formulations. This analysis revealed potential bio actives within Triphala and their known targets) providing hints of the multiple mechanisms potentially working synergistically. The Triphala-cancer network analysis also suggested that ellagic acid, quercetin, and epigallocatechin 3-gallate play a major role as part of the active therapeutic mechanisms of the Triphala for use in cancer. Network pharmacology provides an ethnopharmacological approach to determine the interactions between bioactive agents in herbs, investigate unexplored molecular targets, and find potential drugs from natural sources.

### 2.4. Clinical research in ayurvedic herbal products

Documented clinical trials in Ayurveda for cancer are limited. The US- National Institutes of Health site, ClinicalTrials.gov, lists 47 clinical trials (2000–2022) for "Ayurveda" for multiple disease conditions but only a few for cancer. The trials are mostly in India, Germany, UK, and a few in the USA. These include treatments for COVID-19, sports injuries, coronary artery disease, diabetes, fibromyalgia, chronic kidney disease, knee osteoarthritis, stress, inflammation, immune cell activation and cancer survivorship.

Several clinical trials using Ayurvedic herbs for non-cancer diseases have shown efficacy for knee osteoarthritis, (*Tinospora cordifolia, Zingiber officinale, E. officinalis, Boswellia serrata), glucosamine*) [37]; diabetes, (*Salacia oblonga root, T. cordifolia stem, Emblica offinalis-Gaertn, C. longa, and Gymnema Sylvestre*) [38]; and ulcerative colitis (curcumin) [19]. A standard double-blind, RCT study of rheumatoid arthritis compared methotrexate (MTX) to a classic Ayurveda approach using multiherbal compounds [39]. They found that the effects were equivalent in efficacy plus the adverse

events were fewer in the Ayurveda-only group. This trial represents an example of how clinical trial methodologies can account for complexity of Ayurvedic interventions as well as personalized approaches [40].

A good clinical representation of the holistic approach of Ayurveda in clinical trials for cancer was a whole systems nutrition and lifestyle intervention for breast cancer survivors [41]. This study showed the feasibility and acceptability of an Ayurvedic intervention and measured symptoms and quality of life outcomes. As a pilot study, it was not designed to prove efficacy and warrants further research including optimization of the interventions.

Ayurveda emphasizes restoration and healing [42] and can be used in conjunction with disease-modifying treatments. Preliminary clinical evidence supports the use of some therapies, such as ginger for preventing chemotherapy-induced nausea and vomiting [43] or Indian frankincense (*B. serrata*) for reducing radiation-induced cerebral edema in the brain [44] although more studies are needed to support these findings.

## 3. Research challenges and opportunities for ayurvedic herbs and rasayanas

The Ayurvedic pharmacopeia provides a large resource of herbs and formulations for investigation into health applications. Safety and efficacy of these products are research priorities. It is often misconstrued that if a product is "natural" then it is safe. Some of these 'traditional' herbs have been used over millennia, but studies in safety and efficacy are still critical, especially in the context of potential interactions with current drugs.

By increasing our knowledge of molecular mechanisms along with how Ayurvedic herbs have been used traditionally and clinically over the centuries, we may discover not only new molecular targets or new cellular and systemic pathways used by herbal compounds, but also, we may discover emergent interdisciplinary mechanisms of health. 'Emergent' meaning the discovery of yet unknown pathways or combination of pathways used by traditional herbal compounds, or how these herbal combinations may simultaneously target multiple diseases.

Research approaches for evaluating this botanical resource include ethnopharmacology of traditional medicines and "Reverse Pharmacology" for natural product drug discovery [45]. Also "ayurpharmacoepidemiology" was developed from the collaboration of the fields of clinical pharmacology, epidemiology, and Ayurveda [46]. This effort would examine the effects of Ayurvedic medicinal products on large populations to describe and analyze the practices, evaluate the safety and efficacy, and carry out medico-economic evaluations.

This review has focused on a few herbs from the Ayurvedic tradition, and their specific mechanisms as seen from the reductionist perspective. But the Ayurvedic approach is not to use herbs as magic bullets, like drugs. Ayurveda treats the whole person, not the disease. It provides personalized interventions for the mind and the body based on balances and imbalances of the *doshas* in the ecological milieu of each person. It suggests routines, diet, herbs, and guidelines for specific body types for purification of accumulated toxins, and for strengthening digestion and building immunity. Ayurveda's therapies are simple, self-empowering and target natural processes that help the body heal itself. This includes eliminating the causative factors (wrong diet, disordered routine, addictive habits), purifying the body of accumulated *Ama* by detoxification procedures, incorporating appropriate routine and diet for one's *Prakriti*, and by using stress reduction techniques. Additionally, specific herbs are used to pacify the *doshas*, build immunity and reduce inflammation.

### 3.1. Research gaps: herbs

What are the contributions of this herbal tradition towards understanding cancer pathogenesis and for use in prevention or clinical care of cancer patients? The questions proposed here relate to the use of herbs on different physiological systems related to cancer and are applicable to other diseases such as chronic inflammatory disorders. These represent some research gaps and ideas for further preclinical or clinical investigations:

1. What are the appropriate clinical trials methods to determine efficacy and safety of Ayurvedic herbs in cancer prevention or strengthening the body post treatment?
2. What are the effects of herbs on the level of the tissue microenvironment?
3. What are epigenetic mechanisms of Ayurvedic herbs and modalities related to lifestyle and diet?
4. Many *Rasayanas* are described as 'immune boosting', or as "adaptogens". What are the cellular and molecular targets of this concept and what are the effects of these herbs on the immune system?
5. What can we learn from the traditional combinations of the chemical constituents of the *Rasayanas*? (Network pharmacology) How do these individual agents work together to create novel emergent mechanisms?
6. Could we develop a multiplex 'AyuArray' for biospecimens from patients undergoing Ayurvedic treatments to analyze epigenetics, microbiome, hormones, immunophenotype and metabolomics and potentially discover new mechanisms and pathways?
7. We need better understanding of Herb–Drug interactions. When is an herb or *Rasayana* counterproductive to chemotherapy or radiation and when is it supportive of normal tissues?
8. Also necessary is the standardization of herbal preparations and ingredients across providers.
9. What research methodologies are best suited for evaluating complex mechanisms of whole systems?

Methodologies for clinical trials of these botanicals in combination with standard of care treatment is an area that needs increased activity and development.

## 4. Review summary

### 4.1. Research programs in ayurveda: gaps and opportunities

The aim of this two-part review has been to educate biomedical research scientists about Ayurveda and its potential for integration into current health care studies especially for cancer research. It has provided some stimuli towards developing research programs to grow the evidence for the use of Ayurveda as adjuvant therapies, rehabilitation and palliative care for cancer patients. It has provided an overview of concepts from Ayurveda that can be developed as a scientific evidence-based medicine and to encourage development of statistically strong and reproducible research methods into integrative clinical care programs and health maintenance protocols. This manuscript has reviewed some of the research in Ayurvedic herbs and the traditional tenets of *Prakriti*, digestion, *Agni*, and *Ama* and the realm of mind, body, and spirit or consciousness, and their practical applications to cancer research. The intention is to inspire an open-minded conversation, with debates between Ayurvedic practitioners, basic scientists, and clinicians for possible connections of Ayurveda and western medicine and to correct misunderstandings..

### 4.2. Ayurveda unfolds increasing complexity of targets in cancer research

The focus of cancer research has evolved over the last 50 years. Initial studies discovered altered molecules and pathways in cancer cells and developed specific drugs for each targeted pathway. Further research has unfolded increasingly more complex layers of regulation of cancer cells by the tissue microenvironment, the extracellular matrix, and the surrounding stroma including fibroblasts and immune cells and the gut microbiome, Also involved are the roles of mental stress, and the integrated systems of psychoneuro-endocrine immunology (as discussed in Part 1) [47]. These increasingly complex layers of regulation of body systems underscore the concept of the systems ecology of the body. Ayurvedic principles outline even more complex levels of regulation of how the cells and tissues interact with and are influenced by the elements in nature such as earth, water, fire, air, and space and their role in the doshas: vata, pitta and kapha. Ayurveda equates the human body to an ecological system, aligned with the earth's ecosystem, and the universal laws of nature. Research studies in this area may unfold how wrong diet, behavior and environmental factors provoke an imbalance in the expression of the *doshas* and further affects the physiology and psychology.

### 4.3. Experimental methodologies need to evolve

Our current reductionist methods of research are limited for this personalized, multimodal approach to health. We lose mechanistic information when we try to extract one active agent with a singular mechanism from an Ayurvedic formulation composed of many herbs, each with many compounds. Methodologies are needed to determine mechanisms of synergy in herbal compounds of traditional medicine modalities. In this light, a workshop in 2018 collated a summary of appropriate practices and methodologies for translational research aiming to bring natural products to the clinic (see Sorkin et al., 2020 [48]) Also the US-NIH National Center for Complementary and Integrative Health (NCCIH) has championed development of whole person health research approaches within their strategic plan to bring investigational tools to the research community [49].

Future designs of clinical research in Ayurveda need to account for the complexity due to personalized interventions based the individual body types, or *Prakriti,* of the patients, a critical tenet of Ayurveda. Clinical assessment of *Prakriti* needs to be standardized and transparent in research reports. Clinical study designs should follow guidelines with established human subjects research protocols and be supported by preliminary data of proper dosing, bioavailability, pharmacokinetics, and biomarker correlative studies. Other strategies for developing research programs for Ayurveda are offered by Chauhan [50] and Gautama [40].

A conflicting argument is that there is the possibility that some mechanistic studies in Ayurveda may not find significant differences or efficacy in outcomes or may even find detrimental, unsafe, or toxic combinations with the herbs or treatments. Therefore, unbiased approaches are necessary to accept any outcome. It is also important to consider a perspective from some Ayurvedic practitioners that the approaches of Ayurveda should not be compromised to conform to protocols of reductionist research methods [51]. Some of the non-physical tenets and theories in Ayurveda may not be amenable to mechanistic research as the endpoints are subjective, abstract, or intangible and not able to be quantitated, such as mental aspects of consciousness, measuring increases or movements of the *doshas*, or validating pulse diagnosis. Also, our attempts to integrate Ayurveda into today's oncological treatment methods have often led to misleading translations of ancient Ayurvedic texts. As suggested by Davey, 2017: “It may be helpful retreat to the literary translations of Ayurvedic texts, perhaps with footnotes to explain correlations with modern biomedicine rather than translating Ayurvedic words directly into modern biomedical contexts” [52].

### 4.4. Developing translational integrative research programs in Ayurveda

To build an international research program in Ayurveda, we need to build collaborations between open-minded expert researchers and practitioners from Ayurveda, conventional biomedical scientists, and bioinformatics experts to share ideas and develop a path for practical applications of this knowledge. Towards this point, collaborations between the US and Indian scientists and Ayurvedic scholars and practitioners have been established [53]. The goals are to provide education and explore potential research applications of Ayurveda with mainstream medical practices in US and India. Reciprocal efforts would encourage the theories of Ayurveda to be presented in medical schools where physicians and biomedical researchers can learn the principles and have hands-on training. As well, training could be available to Ayurvedic practitioners and clinicians for advanced research methodologies and to incorporate scientific rigor, reproducibility, and documentation into their studies. Consistency in training of Ayurvedic practitioners has been addressed in an effort by the World Health Organization to develop standardized training guidelines [54].

## 5. Opportunities

It is timely that the vast pharmacopeia and principles of this ancient science can now be explored with current technologies of systems biology to define new cellular, molecular, and immune factors of health and disease. This approach may shed light on mechanisms of Ayurvedic theories and treatments as well as discover emergent mechanisms not previously appreciated. It can also uncover shared physiological processes that underlie the development of diseases whether cardiovascular, musculoskeletal, diabetes, mental health, or cancer.

This effort can assist the development of paradigm-shifting whole person health research approaches, and novel biomarkers for wellness and disease as well as provide new clinical targets to integrate into existing standard of care protocols of current cancer care and other health conditions.

It is important to restate that the use of Ayurvedic modalities should not be used as a substitute for allopathic treatments of cancer. It may support patients after allopathic treatments of surgery or chemotherapy, and in palliative care [55]. Developing a research program to bridge conventional medicine and Ayurveda will help to bring quality and precision to strengthen Ayurvedic research [56]. In summary, Ayurvedic principles and modalities provide an integrative approach which focuses on restoration and healing and may have efficacy in prevention and care of cancer and chronic diseases.

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## Disclaimer

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