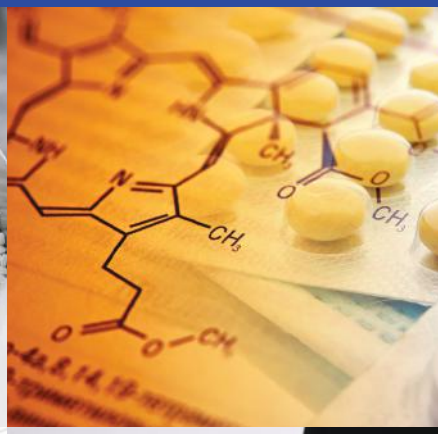
Clinical Aspects of Functional Foods and Nutraceuticals



Edited by
Dilip Ghosh
Debasis Bagchi
Tetsuya Konishi

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2 Clinical Perspective of Ayurceuticals

Challenges and Opportunities for Global Health and Wellness

Namyata Pathak, Hiteshi A. Shah, and Ashok Vaidya

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2.1 INTRODUCTION

> "The power of traditional food formulations is simply phenomenal. The question is, have we capitalized it fully? What about the health aspects of traditional foods, marketing and consumer preferences? Are we adapting the energy-saving processing equipments? Are we changing …?"[1]
>
> **V. Prakash**
> *International Society for Nutraceuticals, Nutritionals and Naturals*

It has been often observed that when two streams of knowledge intermingle, there are chances of major discoveries and development. However, when systems based on diverse epistemology have to mutually enrich their concepts, practices, and products, a major attitudinal shift and a change in world views of the participants are required. Such a change is much more needed when there is a global disenchantment with modern drugs of chemical origin. The prevalent pharmacophobia is primarily due to reports of severe and sometimes life-threatening adverse reactions to these drugs. The numbers of severe adverse drug reactions and the resultant morbidity and mortality have been alarming.[2] As a consequence, there is a movement of "back to the nature," and an aptitude for "green medicine." The emergence of dietary supplements, nutraceuticals, and functional foods has progressed rapidly over the past few decades. The Dietary Supplement Health and Education Act (DSHEA) of the US Food and Drug Administration (FDA) has been a mixed blessing. It has popularized phytoproducts of other cultures but neglected the very systems from which they were derived. All dietary supplements carry the disclaimer: "This product has not been evaluated by the FDA." However, when adverse reactions such as hepatotoxicity of *Piper methysticum*[3] and cardiotoxicity of *Ephedra sinica*[4] emerge, the dietary supplements are promptly banned and warnings issued.

These occurrences are primarily due to isolation of these products from their matrix in the systems of medicine, disregarding the cautions, dosage, indications, and so on, mentioned in the traditional system. It would only be rational to explore and understand the traditional use of naturals and nutritionals of these systems for avoiding such reactions. Though Ayurveda and traditional Chinese medicine offer a vast potential for innovation in nutraceuticals and functional foods, it is vital that precise guidelines and data substantiating health claims are evolved. In India, the new Food Safety and Standards Authority of India (FSSAI) guidelines do not permit disclaimer like that issued by the FDA.[5] Notwithstanding significant and useful guidelines, bureaucratic interference and delays have thwarted the progress and market growth of nutraceuticals in India.[6]

2.2 AYURVEDA

Ayurveda is an officially recognized system of health care in India, which has been practiced for millenia. In a recent survey of the utilization of traditional system in National Rural Health Mission, it was found that 80%–100% of population in 14 out of 18 states used low health tradition (LHT). Even in the states such as Tamil Nadu, Kerala, and Karnataka, with higher per capita income, nearly 50%–75% usage of LHT was reported.[7] Interestingly, it was found that 55% of allopathic practitioners advised LHT in addition to modern medicine and 75% of the practitioners felt that Ayurveda was not a redundant and suggested way of strengthening it. Two volumes of a comprehensive status report on the system have recently been prepared by Dr. Shailaja Chandra, ex-secretary, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Government of India.[8] In view of the long usage and safety of many edible plants with health benefits, Ayurvedic *materia medica* and compendia offer significant opportunities for innovative research and nutraceutical development.[9]

2.2.1 A Nutrition-Centered System

Ayurveda as a holistic system of health, wellness, and longevity was founded upon the *Panchamahabhuta* theory. This theory explains the evolution of microcosm as well as macrocosm. The dynamic exchange of the fundamental elements between the body and its milieu formed the

basis of the *Tridosha* theory (*vata*, *pitta*, *kapha*) and their harmony or imbalance. An individual's constitution too is based on the dominance of the basic elements. This was influenced by the nutrition of parents before conception, after conception, and in the early infant nutrition. Minute attention to the compatibility of natural nutrients and the constitution (*prakruti*) of a person forms the strength of Ayurvedic system.

A new science of nutrigenomics is being correlated with *prakruti* and *pathya*. In Ayurveda, nutrients suitable for an individual are called *pathyas*. Lolimbarāja,[10] a physician poet, in the sixteenth century described their role in health and disease in a verse: "If one eats the right kind of food, what is the need of medicine. If one doesn't eat the right kind of food, how will medicine help?" As Ayurvedic nutrition evolved, various ingredients, methods, and processes were incorporated in texts such as *Ksemakutuhalam*, which deals with food-based products.[11] The guiding wisdom of Ayurveda and scientific advances can be fused pragmatically with modern health care. Such a change is seen at the clinical level as functional medicine, integrative Ayurveda, and integrative medicine.

2.2.2 Global Contributions

Ayurveda was globalized millennia back by Indian universities, namely, Nalanda and Takshashila, where students from many countries came to study. *Charaka Samhita*, the major clinical textbook on Ayurveda, was translated into Greek by Ctesias of Cnidus, a contemporary of Hippocrates—the father of medicine. Greek, Arabic, and Chinese travelers to India carried back the knowledge of Ayurveda globally. In the third century BC, Theophrastus, a Greek botanist, included many Ayurvedic plants in his book. The plants from India formed the constituents of European herbal lore. In the sixteenth century, Garcia d'Orta, a Portuguese physician to the governor of Goa, wrote a book *Drugs of Hindustan* that was translated in seven European languages. He had learnt Ayurveda from two contemporary vaidyas. Many of these plants moved into active *materia medica* of Europe.

In a classical textbook of pharmacology, such as by Goodman and Gillman, the roots of several modern drugs have been traced to several Ayurvedic plants.[12] Such discoveries have also occurred in recent times. Hence, it may still be possible to find other beneficial interventions derived from plants. It is interesting to note that the plant-based drug discoveries in the West were founded upon potent biological effects, which were often poisonous in nature, for example, arrow poison. Once the mechanisms were understood, they were used advantageously for new drugs.[13] Unlike some medicinal plants, which have "poisonous" effects, many more have regulating or modulating effects. Plants are suited for their synergistic effects in disease management, preventive effects in high-risk conditions, and health-promoting effects.

2.3 INNOVATIVE RESEARCH APPROACHES IN AYURVEDA DEVELOPED IN INDIA

Recently, there has been a renaissance in research approaches in Ayurveda. India, over the past few decades, has unraveled ways to use Ayurveda's fundamentals for creating scientific products and services. Ayurvedic pharmacoepidemiology and observational therapeutics have emerged as research approaches for developing new products.[12,14] Reverse pharmacology (RP) too has evolved as an innovative way for product development. Pioneered in India (by one of the authors, Vaidya A.B.V.), it is a science of integrating the documented clinical and experiential hits into transdisciplinary exploratory studies and further developing these into drug candidates by experimental and clinical research. Its scope is to understand the mechanisms of action at multiple levels of biological organization and to optimize safety, efficacy, and acceptability of the leads in natural products based on relevant science. RP was initiated in a study of *Rauvolfia serpentina* in hypertension by Kaviraj Gananath Sen. Reserpine, an active molecule of the plant, was used as a tool to understand

depression, Parkinson's disease, peptic ulcer, and galactorrhea in terms of the biogenic amines. Innumerable new drugs emerged as a consequence.

The global emergence of transdisciplinary clinical pharmacology, the nature of statistical evidence, and the defined targets of drug action preceded the organized endeavor of RP. The bedside screening of Ayurvedic drugs with a benchside follow-up was evolved by Antarkar, Vaidya, and Joshi in the late 1960s. These efforts in diabetes, Parkinson's disease, and hepatitis were quite fruitful.[15,16]

Recently, two major Government-supported activities have been initiated in India: the Council of Scientific and Industrial Research—New Millennium Indian Technology Leadership Initiative (NMITLI) project and the Indian Council of Medical Research (ICMR) Advanced Centre for Reverse Pharmacology in Traditional Medicine (IACRIT). The former was a nationwide multicentric initiative to develop world-class products inspired from Ayurveda. For this, clinical hits for arthritis, hepatitis, and diabetes were identified based on historical evidence and consensus from contemporary practitioners. However, the IACRIT was a center focused on RP for finding the discipline in areas such as malaria, cancer, sarcopenia, and cognitive decline.[17] Some of the products developed through RP have the possibility of being recognized under novel regulatory categories of Ayurceuticals (under the Food Safety and Standards Act, 2006) and phytopharmaceuticals (under the Drug Controller General of India). Such a potential has led to much industry interest in the RP path (Figure 2.1). With a need to develop Vaidya scientists, who would be Ayurveda doctors trained in basic life sciences, a fellowship program has been initiated at the Institute of Ayurveda and Integrative Medicine by the Department of AYUSH.[18]

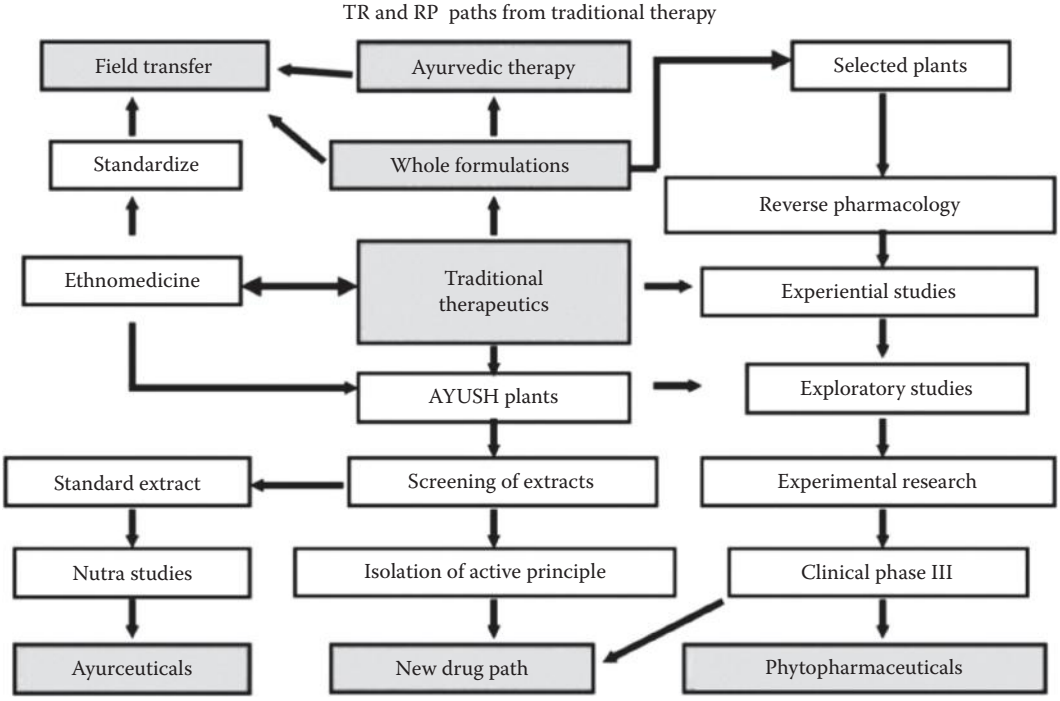

FIGURE 2.1 Development paths in traditional medicine. AYUSH, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy; RP, reverse pharmacology; TR, translational research. (Adapted from Vaidya, A.B., *Proceedings of ICMR Thrust Symposium on Translational Research and Reverse Pharmacology*, Mumbai, IACRIT, Kasturba Health Society, May 31, 2012, p. 124.)

2.4 AYURCEUTICALS

2.4.1 Terminology and Definitions

Ayurceuticals are culture-specific food supplements from Ayurveda, Unani, and Siddha systems. Their scope is to provide for some of the unmet needs of the health care, namely, care of the elderly, metabolic and degenerative diseases, promotion of health and cognitive development of children, and complementary therapy in cancer, allergy, and immune disorders.[19] The spectrum covering Ayurceuticals can be fairly wide as the inspiration for the product is from the wide Ayurvedic usage and categories. Specific food and nutraceuticals can be evolved as per the need and convenience of the user.

Similarly, *rasayanas* can be identified for specific systems or for the whole body. Ayurveda has an in-depth knowledge of taste, properties, and actions of foods *vis-á-vis prakruti*. Ayurceuticals can also be evolved for the reversal of cardiovascular risks or as a complementary to disease management.[20] In Ayurveda, the gastrointestinal (GI) tract is described as "*Mahashotas*, the great stream or path." Its dysfunction leads to several cardiovascular risks. The current developments in gut biota and microbiome open up new opportunities for products such as prebiotics and probiotics, which influence the gut flora.

2.4.2 *Raison D'Être*—Transcultural Challenges

Over the past five decades, botanical product development has been pursued predominantly through phytochemical standardization and screening with biological models of diseases, as defined by contemporary medicine. While this is integral to the process of Ayurceutical development, what strikingly seems amiss is the use of Ayurvedic properties and determinants of clinical response. Such reasoning in the process of product development can enhance their diverse forms, deliveries, and desirable effects, as well as their safety.

A major Ayurceutical example is *Mucuna pruriens*, a natural source of levodopa, which was found to be beneficial in Parkinson's disease in 1978. A further cascade of clinical studies ensued, demonstrating efficacy and certain advantages over the synthetic levodopa supplementation—the mainstay of Parkinson's disease treatment. Consequent global attention to *M. pruriens* has led to products in the markets containing 3%–60% of levodopa (Table 2.1). In Ayurvedic

TABLE 2.1
Some Available Products with *Mucuna pruriens*

Company	Levodopa (%)	Dose Recommendation	Cost ($)
Abhinav	Not mentioned	Two tablets of 300 mg twice a day with a glass of water along with meals	Not mentioned
Himalaya	Not mentioned	One capsule twice a day after meals	71.85/60 capsules
Natural Remedies	10	2 g/day in divided doses	Not mentioned
	20	1 g/day in divided doses	
Sami Labs	10, 15	–	–
Zandopa	Not mentioned	6.525 g in a flavored base; dose as prescribed by physician In half a glass of water (~100 ml) suspend prescribed dose powder, stir, and drink immediately	13.95/175 g
Global Supplements	50	One serving = 1 g, no dose recommendation	99.95/120 servings
Herbal Powers	60	100 mg, one to two times a day, 30 min before meals	35/120 capsules
Ray Sahelin	15	One capsule of 200 mg, in the morning, a few times a week or as directed by your health-care provider	14.95/60 capsules

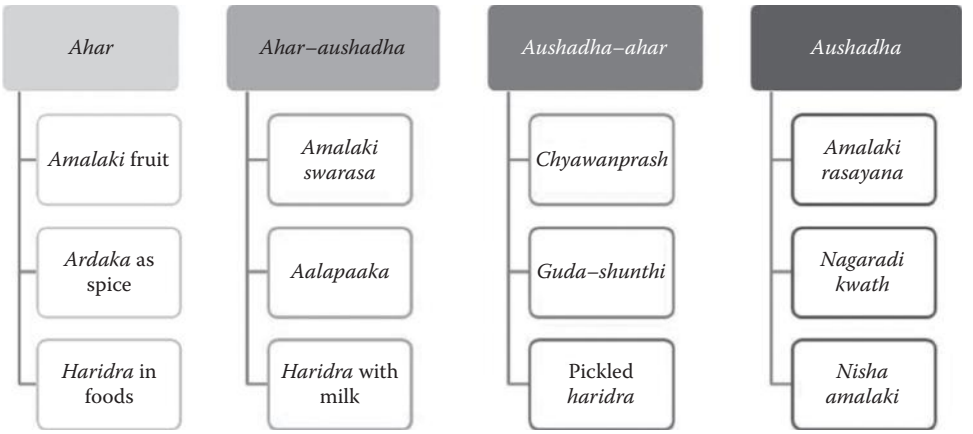

FIGURE 2.2 Food–medicine spectrum in Ayurveda.

formulations, the variations in the composition, processing, dosing, and price are sizable. The strain of *Mucuna* spp., the method of extraction, and the extractive values are mostly not mentioned. Clinical evidence cited is often for a different interventional agent than the one marketed. The dosage forms are not similar to the classical literature or as in the common practice of vaidyas. In addition, in the case of the elderly, the Ayurveda uses *Mucuna* as a jam-like *chyawanprash* or uses it with milk. In these cases, the products are likely to be designed differently for specific health benefits.

Safety should be paramount in using medicinal plants such as *Mucuna*, which are considered as drugs in Ayurveda. It is obvious that the safety index of plants such as *Phyllanthus emblica* and *Curcuma longa*, which are used in diet, would be more than those such as *M. pruriens* used for specific medical and health needs alone. For example, in 1989, when a wild variety of *M. pruriens* was consumed as food during a famine in Mozambique, 203 cases of acute toxic psychosis were reported.[21] Also, dihydroxyphenylalanine (DOPA)-containing *Mucuna* powder, if ingested with a nonselective monoamine oxidase inhibitor (MAOI), can potentially result into a crisis. Hence, when extractions are carried out, the analysis of the sample is desirable but rarely done.[22]

2.4.3 *Ahar* and *Aushadhis*

Ayurveda has dwelt at length on the varying potential of diverse ingredients across the plants. For example, while *Emblica officinalis* as a whole could be consumed as a food, the juice of *Amalaki swarasa* is used as a supplement in diabetes mellitus. For healthy aging, it was converted into a formulation popularly known as *chyawanprash*, but the *Amalaki rasayana*—where the processing includes giving *bhavana* of *Amalaki swarasa* to *Amalaki* powder repeatedly seven times—is being used as a popular complementary treatment of cancer.[23] Similarly, ginger is used as a kitchen spice, but a sweet preparation is used to nourish and strengthen while increasing the *agni*. *Guda shunthi* is used in cold climate, although a special method of consuming the combination is also used to treat odema. Figure 2.2 shows the food–medicine spectrum.

2.5 CLINICAL PERSPECTIVES ON PRODUCTS

Several products from Ayurveda have been used popularly and widely for decades. Here, we share some products that have helped fill certain therapeutic gaps. The basic premise for development of these products had been clinical observations of vaidyas and application of

TABLE 2.2
Examples of Leading Nutra Brands from Ayurveda

Ayurveda Product Brand	Company	Indication	Channel
Liv 52	Himalaya	Hepatitis and liver dysfunction	Consumers and doctors
M2-Tone	Charak	Menopause and menstrual irregularities	Vaidyas and gynecologists
Pancharishta	Zandu	Dyspepsia and flatulence	Vaidyas and consumers
Hajmola	Dabur	Dyspepsia and indigestion	Consumers
Dr. Mom's cough syrup	J.B. Chemicals	Cough	Consumers

TABLE 2.3
Examples of Leading Nutra Ingredients from Ayurveda

Nutraceutical Ingredient	Indication	Related Activity Studies	Product Examples
Aloe vera	Hepatitis	Hegazy et al.[24]	Kumari Asava, Kumaripak
Karela (*Momordica charantia*)	Diabetes	Tsai et al.[25]	Karela (Himalaya), Karela chips
Chyawanprash	Immunity	Parle et al.[23]	Swamla (Dhootpapeshwar), Rajwadi chyawanprash, chyawanprash granules, sugar-free chyawanprash (Dabur)
Brahmi (*Centella asiatica*)	Memory and cognition	Stough et al.[26]	Brahmi prash, Saraswatarishta, Brahmi Ghrita, Brahmi Taila
Vasa (*Adhatoda vasica*)	Cough	Gandhi et al.[27]	Vasavaleha, Vasarishta, Vasakasav, Vasapanak, Vasachandanadi taila, Vasaghritam, Vasaputapak, Gulkand of flowers

technology to create quality products. These are accessed mostly through over-the-counter channels. Recommendations from Ayurvedic physicians and general physicians are often taken. On occasions, conventional specialists do recommend them. The efforts to bring more science to the products are essential for them to be mainstreamed. Their popularity in the market place is a reason for a closer look for their global extension. Table 2.2 lists some Ayurvedic brands that are widely used for indications mentioned and Table 2.3 lists several Ayurvedic plants that are the major ingredients for the specified indications.

2.5.1 GI Wellness

Gut health lies at the heart of Ayurvedic approaches. It is *agni*, the digestive fire essential for the well-being of an individual. Diseases are considered to arise out of vitiations of *agni*. Ayurveda has made available terminology for diseases affecting the GI tract. *Ajirna* (indigestion), *amlapitta* (hyperacidity), *atisaar* (diarrhea), *grahani* (malabsorptive disorders), *aamashaya gata vata* (*vata* in the stomach), *pakwashaya gata vata* (*vata* in the colon), and *chhardi* (vomiting) have been described well with their subtypes. In the Orient, the traditional Asian medicine is often resorted to for relief of the GI complaints. For instance, *shankh vati* is a popular formulation for indigestion, flatulence, and pain in the abdomen. There is room for formulations such as *bilvaavaleha*, a jam of fruit of *Aegle marmelos*, for the irritable bowel syndrome. *Shallaki* is useful in inflammatory bowel disease. Long-standing hyperacidity is managed with *sootshekharrasa*. Table 2.4 describes the four plants used for GI disorders.

TABLE 2.4
GI Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties[28]	References
Ginger (*Zingiber officinale*)	Nausea and heaviness after meals	*Laghu*, *Ushna*, *Snigdha*	Leake et al.[29]
Yashtimadhu (*Glycyrrhiza glabra*)	Heart burn and epigastric discomfort	*Guru*, *Sheeta*, *Snigdha*	Wittschier et al.,[30] Fukai et al.[31]
Shallaki (*Boswellia serrata*)	Inflammatory bowel disease	*Laghu*, *Sheeta*, *Ruksha*	Joos et al.,[32] Gupta et al.[33]
Bilwa (*Aegle marmelos*)	Irregular bowel movement, gaseousness, and irritable bowel syndrome	*Laghu*, *Ushna*, *Ruksha*	Behera et al.,[34] Jindal et al.,[35] Dhuley et al.[36]

2.5.2 Hepatobiliary Protection

Fatty infiltration of liver affects one-fourth of the population. The liver, known as *yakruta* in Ayurveda, is considered central for digestion. Liver health is considered essential in Ayurveda *vis-à-vis* immunity, blood purity and quality, cognition, and musculoskeletal function. Medications such as bitter tonics and common prescriptions such as *arogyavardhini* and *kutki-chirata* help to improve digestion through enhanced liver function. Table 2.5 describes the hepatoprotective plants.

2.5.3 Energy and Metabolism

Despite the adequate intake of substrates for conversion to energy, obese patients complain of low energy and feel fatigued. Ayurveda primarily aims to correct *agni*, albeit at the tissue level, called *dhatwagni*. The corrective agents used are different from those used for *agni* at the GI level. *Santarpana* and *apatarpana* are two opposing ideas of anabolic and catabolic treatments, respectively, which enhance the understanding of *agni* at different levels. The Ayurvedic plants and their ingredients work at the protection of pancreatic islet beta cell mass, prevention of glucolipotoxic damage, and insulin sensitization. Table 2.6 lists the three plants and one medicated wine that will enhance energy and metabolism.

TABLE 2.5
Hepatoprotective Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Kutki (*Picrorhiza kurroa*)	Fatty liver	*Ruksha*, *Laghu*	Shetty et al.[37]
Bhui amalaki (*Phyllanthus amarus*)	Viral hepatitis	*Laghu*, *Ruksha*	Thyagarajan et al.[38]
Trikatu (*Zingiber officinale*, *Piper longum*, *P. nigrum*)	Liver-related dyspepsia	*Laghu*, *Ushna*, *Tikshna*	Johri et al.[39]

TABLE 2.6
Energy/Metabolic Plants

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Amalaki (*Phyllanthus emblica*)	Pancreatic salvage	*Guru*, *Ruksha*	Balu et al.[40]
Mamejava (*Enicostemma littorale*)	Glucotoxicity	*Laghu*, *Ushna*, *Ruksha*	Vaidya et al.[41,42]
Methi (*Trigonella foenum-graecum*)	Insulin resistance	*Ushna*, *Snigdha*, *Laghu*	Gupta[43]
Drakshasava (classical formulation)	Fatigue	*Snigdha*, *Ushna*, *Laghu*	Sharma[44]

TABLE 2.7
Musculoskeletal Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	References
Ashwagandha (*Withania somnifera*)	Muscle weakness	*Laghu*, *Snigdha*	Raut et al.[45]
Guggul (*Commiphora wightii*)	Rheumatic pains	*Laghu*, *Tikshna*, *Snigdha*, *Pichchil*, *Sukshma*, *Sara*	Raut et al.[46]; Chauhan et al.[47]
Rasna (*Pluchea lanceolata*)	Low back ache	*Guru*, *Ushna*	Vaidya and Gogte[48]

TABLE 2.8
Cardiovascular Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Arjun (*Terminalia arjuna*)	Low heart reserve	*Laghu*, *Ruksha*	Dwivedi et al.[49]
Garlic (*Allium sativum*)	Improvement in blood flow	*Snigdha*, *Tikshna*, *Pichchil*, *Guru*, *Sara*	Banerji et al.[50]
Pomegranate (*Punica granatum*)	Antioxidant damage	*Laghu*, *Snigdha*	Kotamballi et al.[51]

2.5.4 Musculoskeletal Health

A focus on muscle health in nutraceuticals was primarily in sports medicine and nutrition. Recently, the mainstream medicine has recognized sarcopenia as a distinct and important problem. *Commiphora wightii*[47] has been explored for hypolipidemic activity, but traditional practitioners use it widely for rheumatic aches and pains. Low back ache has diverse etiology, but its musculoskeletal component can benefit significantly with *Rasna* and its traditional formulations. Table 2.7 shows the three plants of promise.

2.5.5 Cardiovascular Reserves

With global changes in lifestyle and food habits, cardiovascular morbidity and mortality have emerged as formidable challenges. Besides yoga, exercise, and low-fat diet, there is a need for safe plant-based agents to reduce cardiovascular risk factors. Table 2.8 lists the three plants with a high potential for their development as enhancing cardiovascular reserves.

2.5.6 Respiratory Tract

Ayurveda has much to offer for common upper respiratory tract infection. In India, millions of people avail of simple home remedies for common cold and sore throat. However, the major opportunity lies in exploring Ayurvedic plants for enhancing immunity in recurrent respiratory infections and reducing the frequency, duration, and severity of asthmatic attacks. Table 2.9 lists some products with a potential for respiratory Ayurceuticals.

2.5.7 Kidneys and Bladder Disorders

The classical Ayurveda text elaborates conditions such as dysuria, oliguiria, anuria, and calculi. Many Ayurvedic medicinal plants and formulations are recommended for these conditions and are found to be effective. Plants such as *gokshura*[54] and *punarnava*[55,56] are found to be effective in

TABLE 2.9
Respiratory Ayurceuticals

Ingredient	Proposed Nutra Indications	Ayurvedic Properties	Reference
Chyawanprash	Promote respiratory immunity	*Guru*, *Snigdha*, *Ushna*	Parle et al.[23]
Banapsha (*Viola odorata*)	Persistent dry and irritating coughs	*Laghu*, *Ruksha*	Parihar et al.[52]
Sitopaladi (classical preparation—*Mishri, Vanshlochan*, *Piper longum Linn*, *Elettaria cardamomum*, *Cinnamomum zeylanicum*)	Dry and wet coughs	*Laghu*, *Snigdha*, *Ushna*	Sharma[44]
Pippalimoola (*P. longum*)	Bronchial asthma	*Laghu*, *Ushna*	Fernandez et al.[53]

TABLE 2.10
Urinary Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Chandan (*Pterocarpus santalinus*)	Protection from urinary tract infection	*Laghu*, *Ruksha*	Gogte[28]
Punarnava (*Boerhavia diffusa*)	Kidney reserves	*Laghu*, *Ruksha*	Upadhay et al.[55,56]
Gokshura (*Tribulus terrestris*)	Benign prostatic hyperplasia	*Guru*, *Snigdha*	Joshi et al.[54]
Kulathi (*Dolichos biflorus*)	Kidney stones	*Laghu*, *Ruksha*, *Tikshna*	Singh et al.[57]

TABLE 2.11
Psychoneural Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Shankapushpi (*Convolvulus pluricaulis*)	Memory enhancer	*Snigdha*, *Pichchil*, *Guru*, *Sara*	Sethiya et al.[61]
Pippalimoola (*Piper longum*, root)	Anxiolytic	*Laghu*, *Snigdha*, *Tikshna*	Lee et al.[62]
Saraswatarishta (classical formulation)	Promotion of cognition	*Laghu*, *Snigdha*, *Ushna*	Mishra[63]

kidney and urinary disorders. However, plants such as *pashanbhed* and *kulathi* are beneficial in preventing kidney stones.[57] Table 2.10 lists some of these plants.

2.5.8 Psychoneural Health

Ayurveda pays special attention to drugs of the central nervous system (CNS).[59–60] Some of these have been investigated with modern scientific methods. Studies have established the beneficial effects of certain bioactive compounds in medicinal plants, such as memory enhancing, relieving anxiety, and promoting cognition.[59–61] Table 2.11 lists psychoneural Ayurceuticals that highlight the benefits of the bioactive compounds.

2.5.9 Reproduction and Sexual Health

The activities of plants and formulations in sexual health and reproductive disorders were given special attention in Ayurveda as *vrishya dravyas*. Significant research has been initiated in this field. A focused RP research approach needs to be brought to the three plants listed in Table 2.12.

TABLE 2.12
Vrishya Dravyas

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Shatavari (*Asparagus racemosus*)	Galactogogue	*Guru*, *Snigdha*	Jetmalani et al.[64]
Kaunch (*Mucuna pruriens*)	Promotion of virility in the elderly (both sexes)	*Guru*, *Snigdha*	Singh[65]
Ashoka (*Saraca indica*)	Menorrhagia	*Laghu*, *Ruksha*	Pradhan et al.[66]

TABLE 2.13
Immunostimulant Ayurceuticals

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Tulsi (*Ocimum sanctum*)	Prevention of infections	*Laghu*, *Ruksha*	Vasudevan et al.[67]
Guduchi (*Tinospora cordifolia*)	Immunomodulator	*Laghu*, *Snigdha*	More et al.[68]
Daruharidra (*Berberis aristata*)	Antimicrobial	*Laghu*, *Ruksha*	Bhandari et al.[69]
Kiratatikta (*Swertia chirata*)	Postinfection convalescence	*Laghu*, *Ruksha*	Pharmacopoeia of India[70]
Kalmegh (*Andrographis paniculata*)	Antiviral	*Laghu*, *Ruksha*, *Triksna*	Wiart et al.[71]

TABLE 2.14
Ayurcosmetics/Dermatologics

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Khadir (*Acacia catechu*)	Acne	*Laghu*, *Ruksha*	Gogte[28]
Ajmoda (*Carum roxburghianum*)	Skin allergies	*Laghu*, *Ruksha*, *Triksna*	Gogte[28]
Gandhak rasayana (classical formulation)	Adjuvant in skin disorders	*Sheeta*, *Snigdha*, *Guru*	Yogratnakar[72]
Jabakusum (*Hibiscus rosa-sinensis*)	Hair fall	*Laghu*, *Ruksha*	Adirajan et al.[73]
Turmeric (*Curcuma longa*)	Skin allergies	*Laghu*, *Ruksha*	Shishodia et al.[74]

2.5.10 Immunity and Infections

Ayurveda laid great stress on enhancing resistance to infections rather than developing anti-infectives. *Berberis aristata* and *Tinospora cordifolia* have shown remarkable activity as immune stimulants. Tulsi, also known as holy basil, has been used in Ayurveda since centuries. It is a household plant in India and used in ailments such as common cold, headaches, stomach disorders, and malaria. Table 2.13 lists some immunostimulant Ayurceuticals.

2.5.11 Skin, Hair, and Nails

Having realized the negative effects of chemical-based cosmetics, the need for natural products for beautifying skin, hair, and nails is growing. There are standard references, usage, and research on Ayurvedic cosmeceutics for the indications of skin pigmentation, wrinkles, hair fall, freckles, periorbital darkness, acne, skin infections, and so on. Table 2.14 gives a list of ayurcosmetics. There are multi-ingredient hair oils, which are used by millions in India.

TABLE 2.15
***Rasayana* for Aging**

Ingredient	Proposed Nutra Indication	Ayurvedic Properties	Reference
Triphala (classical combination—*Phyllanthus emblica*, *Terminalia chebula*, *Terminalia bellerica*)	Antiaging	*Ruksha*, *Sheeta*, *Laghu*	Singh et al.[75]
Garlic (*Allium sativum*)	Antiaging	*Snigdha*, *Tikshna*, *Pichchil*, *Guru*, *Sara*	Khalid[76,77]

2.5.12 Retardation of Aging

The principle and practice of *kayakalpa* (rejuvenation) is unique to Ayurveda. Ayurveda has a great potential to explain reversal of aging and regeneration of tissues. There are anecdotal reports of reversal of aging in Ayurveda literature, with a regimen of specific medications, milk, and a stay in dark shelter. *Triphala* is widely used as *rasayana* by the aged in India. Table 2.15 lists the two *rasayanas* for aging.

2.6 OPPORTUNITIES AND CHALLENGES

Health professionals and consumers seek a clinical rationale to use a product, besides efficacy with statistical significance. The practice of a long traditional use may generate interest in the ingredients. The backing of contemporary science would enhance the value. This is an opportunity awaiting to be unearthed with the help of a collaborative R&D team.

Reverse nutraceutics is proposed as a new guiding path to create nutra/Ayurceuticals, analogous to what RP has become for modern drug development from Ayurveda. Like RP, reverse nutraceutics has much potential of developing global novel products inspired by products already being safely used in the field (Figure 2.3). Although it is depicted linearly, it may have many feedback loops and would be nonlinear on execution.

As the ingredients for most nutra- and Ayurceuticals are already being used in the field, reverse nutraceutics begins with nutra epidemiology. Through systematic surveys, extensive initial information can be sought: extent of use, safety of use, ease of use, popular practices and processing requirements, modifications used globally, incorporation in daily life, distribution channels, availability, and cost-effectiveness of a potential product (ingredient/formulation). It would also include the study of classical texts and historical evidence of use.

Human observational studies provide case reports or detailed anecdotes of individual experiences by a physician or a sensitive patient. They allow knowing the nature of beneficial response and the temporal relation with intake of ingredient. These are essentially well-described clinical phenomena.

There are three well-designed studies: experiential, exploratory, and experimental.

Experiential nutra studies are open-labeled studies, using common target symptoms and routine investigations as assessments, in a sample group as determined by earlier observations. This stage evolves hits to be taken up further.

Exploratory studies (in vitro, in vivo, *and clinical studies*) need to evolve models and targets relevant to clinically documented effects. The need to innovate models cannot be overemphasized. This stage generates leads from the hits.

Experimental studies (*human nutra studies*) are controlled studies *for* safety and efficacy with defined serving size and defined indications. Experiments for putative mechanistic understanding at all levels of biological organization are included. This stage develops the leads into Ayurceutical candidates.

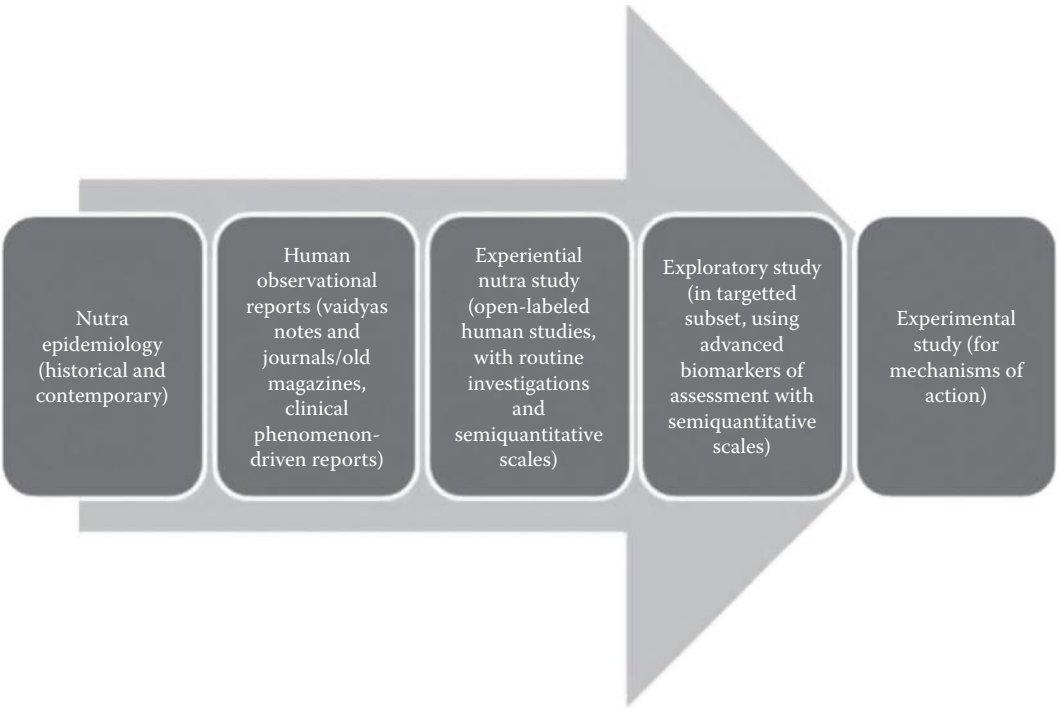

FIGURE 2.3 Reverse nutraceuticals.

The human nutra studies are distinct from drug trials in many ways. The safety of long-term usage in humans provides a comfortable baseline. The range of serving amounts used facilitates dosage. There is also a possibility of a previous field survey of usage (nutra epidemiology), leading to clinically demonstrated effects that guide the development of novel *in vitro* and *in vivo* models.

There is an urgent need of a transdisciplinary team development in Ayurceuticals. The diverse expertises that can be involved are food scientist, food technologist, vaidya partners, nutritionist, botanist, phytochemists, pharmaceutics, pharmacologist, and colleagues. The future of Ayurceutical depends on striving for excellence by such a team.

2.7 CONCLUSIONS

Ayurceuticals are nutraceuticals inspired from the ancient and live system of Ayurveda. The widespread use of Ayurvedic plants makes the potential large. The specific Ayurceutical opportunities, in terms of the plants or formulations, have been listed with appropriate references. It is hoped that reverse ayurceutics from the traditional system of medicine is taken up in earnest within India and globally.

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GLOSSARY

***aalapaaka*:** shredded ginger in boiled sugar confectionery
***agni*:** the digestive fire
***ahar*:** diet
***ahar–aushadha*:** dietary products of medicinal value
***amalaki*:** the Indian gooseberry
***aushadha*:** medicine
***aushadha–ahar*:** medicinal products that can be a part of diet
Ayurveda: an Indian traditional medicine
***bhavana*:** a process in which a medicinal substance is impregnated with the juice of another medicinal substance
***chyawanprash*:** a popular jam used as antiaging formulation and for immune enhancement
***dhatwagni*:** moiety of agni that helps in metabolism at the tissue level
***guda–shunthi*:** combination of jaggery and dried ginger
***guru*:** heavy, that which is digested slowly
***haridra*:** Sanskrit name for turmeric
***kapha*:** one of the three doshas (the vital humors)
***laghu*:** light (guna); easy to digest
***nagaradi kwath*:** a decoction containing dried ginger and other herbs
***nisha amalaki*:** combination of turmeric and amla (the Indian gooseberry)
***pathya*:** regimen of diet/lifestyle in a particular disease
***pichchil*:** viscous, sticky
***pitta*:** one of the three doshas (the vital humors)
***prakruti*:** the original nature, character, constitution, or temper of a person
***rasa*:** juice of any medicine; taste perceived by the tongue; mercury; mercurial preparation
***rasayana*:** antiaging phenomenon or formulation
***Ruksha*:** dry
***Sara*:** fluid, liquid (one of the 20 gunas); cathartic, purgative, laxative
***Sheeta*:** cold
Siddha: one branch of traditional medicine that has flourished especially in South India
***Snigdha*:** oily (one of the 20 gunas)
***Sukshma*:** minute, subtle (one of the 20 gunas)
***swarasa*:** plain juice of any medicine
***Tikshna*:** hot, sharp, fast acting
Unani: one branch of traditional medicine
***Ushna*:** hot, heat
***Vaidya*:** a physician of Indian traditional medicine
***vata*:** one of the three doshas (the vital humors)

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