

Comprehending Ancient Wisdom of Ayurveda: Unveiling Phytochemistry and Molecular Mechanisms of Rasayana Medicine

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Abstract

Rasayana medicine is an integral part of ancient medical system of India. In Sanskrit 'rasayana' refers to "path of essence" and serves as one of the eight clinical specialties of classical Ayurveda. Rasayana focuses on restoring health by replenishing vital fluids of human body. According to Ayurveda, our physical body constitutes of seven dhatus called 'Sapthdhatu', sapth-seven and dhatu-tissues or microchannels. These channels are the pathway through which vital nutrients flows to nourish our bodies. Taking rasayana medicine is dedicated for immune protection, acts as anti-degenerative and rejuvenates health care by alleviating effects of age-related degeneration along with restoring cellular stability in disease and healthy individuals. Therefore, rasayana is a tool to create premium dhatus so when any dis-ease or dishamaony occurs, quality of dhatus promotes rejuvenation, regeneration, healing by enhancing immunity and developmental mechanisms by tuning cellular homeostasis. The phytochemistry and molecular mechanisms lay foundation for the pathways or chemical reactions that will be initiated to provide the endpoints of restoring physical and mental vitality. Rasayana phytochemistry and its molecular action are based on robust correlation between its therapeutic goals and the impact bioactive compounds provides in achieving its observed biological effects. Traditional Rasayana therapies have time-tested system approaches by bridging detoxification or disease healing aspect along with restoring balance and sustaining health. The rejuvenating out-turn of rasayanans stems from their synergistic action of numerous bioactive components which are plant-based. This review article implies understanding role on its phytochemical composition and their molecular mechanisms behind mode of action of rasayana medicine coinciding modern science outview through ayurvedic principles, thus validating its traditional claims.

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INTRODUCTION

Ayurveda is a native traditional medicine system of India. Ayurveda lays foundation for most ancient and living traditions which has been practiced since thousands of years the scientific philosophies and experimental basis. Atharvaveda [1], Charak Samhita [2] and Sushrut Samhita [3] are the classic references that describe detailed descriptions of over thousands of herbs, their preparations and use in treatment of all ailments [4,

5]. Conventional Ayurveda remarks medicine therapy into two sets- Preventive and Curative therapies [6]. Rasayana therapy [7] comes under preventive therapies and is further divided on basis of treatment, administration, utility, mode of action and type of materials used [8–14]. On broader spectrum all these are interconnected.

Based on Place of Treatment

- Kuti Praveshika- the indoor patient treatment
- Vatatapika – outdoor patient regimen

On Basis of Utility

- Kamya Rasayana - for enhancement of normal health. Subdivided as-
- Prankamya- Promoting vitality and longevity
- Medhakamya- for promoting intelligence and memory
- Shrikamya- Promotes complexion, luster and vitality
- Naimittika Rasayana – on basis of disease condition. Rasayana are administered specific to disease.
- Aajasrik Rasayana- use of substances on a daily basis from food for body nourishment. Eg: Clarified butter (Ghee), Cow's milk, honey which helps in promoting immunity and alleviates nutritional disorders.

Based on Mode of Action

- Samshodhana Rasayana- Rejuvenating body by expelling the aggravated doshas.
- Samshamana Rasayana- Rejuvenates body by pacifying accumulated doshas.

On basis of Dravya (substances)

- Dravyabhuta Rasayana – therapy including herbs, minerals and food.
- Adravyabhuta or Achara Rasayana- no substance is used instead modalities like good behavior, meditation and yoga are performed.

On Basis of Drug, Diet and Lifestyle

- Aushadha Rasayana- based on drugs and herbs
- Ahara Rasayana- based on diet and nutrition
- Achara Raayana-specified by code of conduct, behavior and lifestyle.

BENEFITS OF RASAYANA MEDICINE

Rasayana medicine or therapy is one of the integral branches of *Ashtang Ayurveda* [15] showing existence of 'knowledge of branches of science' where each branch is specialized in its own way. Rasayana therapy belongs to 'Jara Chikitsa' the one that explain methods and materials used for vasa sthapan (having anti-oxidant, immunomodulatory, adaptogenic properties [16] forming basis for health and prevention of disease). On a bigger perspective, rasayana branch deals with following physiological and metabolic factors.

Physiological Status

- Vaya (age)
- Prakriti (body constitution)
- Satmya (adaptability)
- Agni (digestive capability)

Metabolic Status

- Dhatus (bodily tissues)
- Ojas (Vital essence)
- Strotas (body microchannels)
- Bala (Strength)

MODE OF ACTION OF RASAYANA THROUGH SAPTADHATUS

AYURVEDA forms foundation of human physiology and pathology by concept of “Saptadhatu”, sapta-seven and dhatu- tissue or microchannels. These seven are the vital tissues that nourish, grow, support, stabilize and provide structure to body. Saptadhatu are foundational structural and functional units of human body. It is the fundamental source which provides strength, energy, nourishment and support to our body. These microchannels are responsible for maintaining cellular homeostasis contributing to health. Any disharmony in formation any of dhatus leads to manifestations of diseases. According to ayurvedic principles, nourishment and tissue formation occurs in a sequential order as follows.

Food->Rasa->Rakta->Mamsa->Meda->Asthi->Majja->Shukra

By focusing on individual cell, tissue-level nourishment model describes macro and micro level system of communication and transformation. Dhatus are-

- Rasa (Plasma/Lymph)
- Rakta (Blood)
- Mamsa (Muscle)
- Meda (Fat)
- Asthi (Bone)
- Majja (Marrow/Nervous Tissue)
- Shukra (Reproductive Tissue)

Each succeeding dhatu is developmental metabolic refinement of previous one. These dhatus replenish, provide strength, integrity and function of body. When these ‘retainable substances’ are expelled from body they become waste matter (Mala).

Waste matter (Mala) naturally occurs as unusable by-products of digestive cellular crosstalk with association to formation of each of Saptadhatu [17, 18]. These can be fecal matter, sweat, urine, mucus, saliva, tears and carbon dioxide.

PHYTOCHEMISTRY OF RASAYANA MEDICINE-

Rasayana medicine in Ayurveda is known for their rejuvenating and health promoting properties. The phytoconstituents responsible for these effects vary depending on their ingredients of formulation. Phytochemistry is a scientific discipline that combines elements of botany and chemistry to study chemical compounds produced by plants in biological action on human body. The phytochemical constitutes of herbal formulation decides their therapeutic action. Phytochemicals are active ingredients possessing biologically natural chemical components from plants such as sugars, amino acids, protein, chlorophyll, alkaloids, flavonoids, steroids, tannins, ascorbic acid [19], etc. A vast array of naturally occurring chemical compounds from plants can be classified as-

- *Primary Metabolites*: are compounds essential for plant's basic growth and survival. Eg- carbohydrates, proteins, lipids etc.
- *Secondary Metabolites*: are compounds that are not directly involved in plant's growth mechanism but are synthesized to deal with important circumstances such as defense against pests, diseases, natural calamities, protection of plant's life. These compounds are responsible for medicinal properties, unique colors, aroma of plants.

Key Classes of Phytochemicals

The phytochemicals are diverse but mainly grouped into classes, including-

- *Alkaloids*: resemble bitter-tasting, nitrogen –containing compounds.
- *Polyphenols*: group of compounds known for their anti-oxidant properties.
- *Flavonoids*: class of polyphenols, contribute to its anti-oxidant and anti-inflammatory properties.
- *Tannins*: polyphenols that affects metabolism or gut microbiota with aim to improve metabolic performance. They have also been reported to show physiological effects.

- **Terpenoids:** responsible for aromas of many plants and their main component are essential oils. Eg- menthol (mint), limonene (citrus)
- **Glycosides:** compounds where sugar compound is attached to a non-sugar molecule.
- **Saponins:** soap-like glycosides that can have wide range of effects from immunomodulation to memory enhancement.
- **Polysaccharides:** long-chain polymeric carbohydrates composed of monomeric units linked by glycosidic linkages. It helps in promotion immune function.
- **Peptides:** short chain amino acids linked together to form blocks of proteins.
- **Coumarins:** polyphenolic compounds well-known for their anti-coagulant action.
- **Thiosulfinates:** compounds responsible their distinctive pungent flavor. Eg- allin from garlic.
- **Volatile Oils:** concentrated hydrophobic liquids containing volatile chemical compounds.

From vast array of herbs mentioned in Ayurveda's Rasayana Chikitsa (Treatment), few of them are listed to showcase presence of their therapeutic phytoconstituents. Table 1: Phytoconstituents of Rasayana herbs.

Table 1. Phytoconstituents of Rasayana herbs.

Plant name (botanical name)	Key phyto chemical constituents
Ahiphena (<i>Papaver somniferum</i> Linn.)	Alkaloids: codeine, narceine, narcotine, morphine, and papaverine (a peripheral vasodilator). Other: bitter principle (meconin), meconic acid.
Gokshura (<i>Tribulus terrestris</i> Linn.)	Alkaloids: harmine and harmaline. Other: steroid saponin (protodioscin), resin.
Kapikacchu (<i>Mucuna pruriata</i> Hook.)	Alkaloids: nicotine, mucuadine, mucunadinine, mucuadininene, pruridine, and pruridinine. Other: L-dopa, glucoside, serotonin, glutathione.
Jatiphala (<i>Myristica fragrans</i> Houtt.)	Volatile oil: myristicin, saffrole, elemicin. Fixed oil: butter of nutmeg.
Shatavari (<i>Asparagus racemosus</i> Willd.)	Steroid saponins: shatavarins. Other: mucilage.
Arkarambha (<i>Anacyclus pyrethrum</i> DC.)	Alkaloid: pyrethrine. Other: resin (pyrethrin), inulin, volatile oil.
Kataphala (<i>Myrica nagi</i> Thunb.)	Glycoside: myricitrin. Other: tannin, volatile oil.
Kokilaksha (<i>Astercantha longifolia</i> Nees.)	Alkaloids: unspecified. Other: mucilage, oil, aliphatic esters, betulin.
Talamuli (<i>Cucurlogo orchoides</i> Gaertn.)	Unspecified: starch, sterols, tannins, ash, oil.
Musali (<i>Asparagus adscendens</i> Roxb.)	Glycosides: spirostanol glycosides (asparain a and b), furostanol glycosides (asparagosome a and b). Other: asparagin, albumin, starch.
Ashwagandha (<i>Withania somnifera</i> (Linn.) Dunal.)	Alkaloids: anagrine, anaferine, cuscohygrine, hygrine, isopellettriene, pseudopellettriene, 3-trotyltigloate, tropine, withasomnine. Withanolides: withaferin-A, withanol. Other: proteins, amino acids, dulcitol, and minerals (iron, potassium, magnesium, nickel).
Amla (<i>Emblica officinalis</i> Gaertn.)	Vitamins: L-ascorbic acid (Vitamin C). Tannins and Phenolic Compounds: emblicanin A and B, gallic acid, ellagic acid, flavonoids (quercetin, rutin). Alkaloids: phyllantine, phyllantidine.
Haldi (<i>Curcuma longa</i> Linn.)	Curcuminoids: curcumin, demethoxycurcumin, bisdemethoxycurcumin. Volatile oils: turmerone.
Shunti (<i>Zingiber officinale</i> Roscoe)	Phenolic compounds: gingerols, shogaols, paradols. Volatile oils: zingiberene, beta-bisabolene, alpha-curcumen.
Lasuna (<i>Allium sativum</i> Linn.)	Organosulfur compounds: alliin, allicin, ajoenes, diallyl sulfide (DAS), diallyl disulfide (DADS). Flavonoids: quercetin.
Shankhpushpi (<i>Convolvulus pluricaulis</i> Choisy)	Alkaloids: convolvine, convolamine, convolvidine. Other: glycosides, coumarins (scopoletin), flavonoids (kaempferol), sterols (beta-sitosterol).

Brahmi (<i>Bacopa monnieri</i> (L.) Wettst.)	Saponins: bacosides A and B, bacosaponins. Alkaloids: brahmine, herpestine. Other: flavonoids (apigenin).
Pippali (<i>Piper longum</i> Linn.)	Alkaloids: piperine (the major active constituent), piperlongumine, piperlonguminine. Other: volatile oils, fatty acids, lignans (sesamin).
Dalchini (<i>Cinnamomum zeylanicum</i> Nees)	Essential oils: cinnamaldehyde (the principal active component), cinnamyl acetate, eugenol, caryophyllene, linalool. Other: cinnamic acid, coumarin (especially in <i>Cinnamomum cassia</i>).
Mandukaparni (<i>Centella asiatica</i> (L.) Urban)	Triterpenes: asiaticoside, madecassoside, asiatic acid, madecassic acid. Alkaloids: brahmoside, hydrocotyline, centelloside. Other: flavonoids, volatile oil.

PHARMACOLOGICAL AND MOLECULAR MECHANISMS OF RASAYANA MEDICINE

Rasayana medicine or rasayana therapy is the “*science of nutrition*”. It is not only a drug therapy but is a procedure practiced to provide proper nutrition at the cellular level through nourishing dhatus. The main objective of rasayana medicine is enhancement of natural immunity, improving functioning of all fundamental organs of body, keeping early symptoms of retarding through ageing at bay. It acts as rejuvenating therapy by achieving cellular homeostasis, dealing with degradation, prevention of diseases and improving the quality of life. The studies done indicate Rasayana plays important role in maintenance and preservation of health along with appropriate administration could help in alleviating prevalence of many diseases [7]. Figure 1: Molecular mechanisms of Rasayana depicting the various aspects of their pharmacological actions.

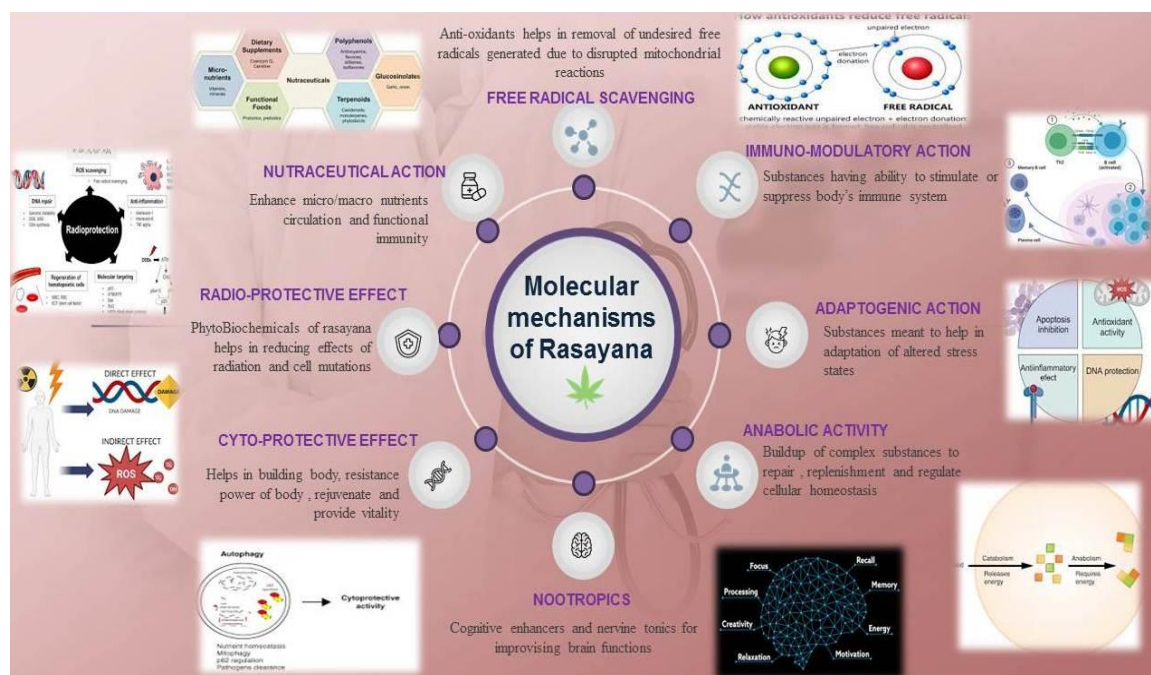


Figure 1. Molecular mechanisms of Rasayana depicting the various aspects of their pharmacological actions.

Health is complex phenomenon maintaining numerous interrelated physiological, biochemical and hormonal functions acting in harmony with precision. Ayurveda explains rasayana medicine as devoted branch for maintenance and promotion of health by revitalizing metabolism, nourishing dhatus, enhancing immunity and therapeutic potential to combat many diseases. Several ancient texts describes benefits of rasayanas and their ethno pharmacology when evaluated clinically, pharmacologically, biochemically and biologically indicates that rasayana does not work on a single activity but on numerous molecular mechanisms at a time [20, 21]. This action varies from compound to compound and their poly-herbal formulations. Most possible mechanisms through which action of rasayanas could be presented in accordance to modern science aspect are.

Inhibition of Free Radical Stress

As part of cellular mechanisms, oxygen radicals are released as stress presenting threat to normal cellular functions. Free radical scavengers also known as anti-oxidants, are the compounds that help in removal of undesired free radicals generated due to disrupted mitochondrial respiratory reactions. Rasayana acts as anti-oxidants which neutralize reactive oxygen species (ROS) during aerobic cellular metabolism. Natural antioxidants from rasayana medicine act as important elements in maintenance and preservation of aging, neurodegenerative diseases, carcinogenesis, hematological disorders and chronic inflammation. Thus, anti-oxidants from rasayana counterbalance by scavenging oxygen free radical molecules and helps in alleviating oxidative stress in the body by acting as anti-oxidative defense system [22].

Immunomodulation Action

Cellular interactions among immune cells with itself and other tissues are crucial process for maintaining health and protection against illness. The substances that have ability to stimulate or suppress body's immune system by affecting some parts of the body that respond to illness, infection or disease are termed as immunomodulators that could be explained by their actions categorized as-

- Immuno-stimulators
- Immuno-suppressors

Immuno-Stimulators

Stimulate term refers to activation. Immunostimulators are components that help in encouraging parts or immune system defense as a whole for regulating functional responses. They are further divided in two classes: a) *specific immuno-stimulators*: facilitate antigenic specificity in immune response such as antigens or vaccines, b) *non-specific immuno-stimulators*: to stimulate components of immune system resembling adjuvants.

Immuno Suppressive

agents that provide prevention against activity of immune system. Mostly used in immunosuppressive drugs in treatment of autoimmune disease, in prevention of rejection of transplanted organs and in non-autoimmune inflammatory disease.

Ayurvedic rasayans are of non-specific type of immune-modulators as they act to strengthen immune system as a whole by increasing quality and quantity of components to level of perfection. Rasayana as immune-stimulant [23] helps in formation of healthy and normal functioning cells in all system of body along with inhibition of metastasis. As immune-suppressants they regulate activities of T cells.

- *Adaptogenic Activity or Anti-stress*: A Russian scientist 'Lazarev' explains concept of adaptogens as substances meant to put organisms into state of non-specific resistance to stress (physically, chemically and biologically) and help in adaptation of altered circumstances. Rasayana behave as adaptogens as they have shown proven results as medically effective substances by modulating body's central stress response system and by strengthening normalizing functions of body and acting as defense systems against variety of environmental stresses [23, 24]. Rasayanas shows two-types of effects: a) it can neutralize negative effects of environment or challenges on physiology by restoring homeostasis, b) by long-term administration person's tolerance gets leveled up. This helps in reducing cumulative chronic stress damage in body.
- *Anabolic Activity*: related to increase in activity of anabolism of the metabolic pathway which in turn increases synthesis of nucleic acid and protein synthesis. Anabolism as a concept is explained by buildup of complex substances. Thus, Rasayana are potent in inducing proliferation and repopulating depleted or worn tissues, replenishing nutritional deficiency and enhancing formation of new tissues for maintaining health by balancing homeostasis [25]. This improves cellular signaling and communication thus leading to optimal nourishment alongwith regeneration of body tissues.

- *Nootropic Effect or Cognitive Enhancer:* The word nootropic is made up from two words: Noos-mind and tropic- turn, meaning “action on mind”. Rasayanas are substances with potency to enhance memory and mental function. They are cognitive enhancers working best as psychopharmacological agents stimulating neural synapses to their optimum performance. They are improvers of integrative brain functions like memory, learning, understanding, thinking and concentration capacities [26]. Rasayana could help in reducing damage due to energy disturbances or neurotransmitter metabolism.
- *Cytoprotective Effect:* demonstrates action of proteins in maintenance of regular functioning for optimum health. Proteins are available in body in particularly two forms: a) tissue proteins: responsible for forming different tissues, b) plasma proteins: consisting of globulins responsible for maintaining body's immunity. Rasayanas improves dhatu formation in the body and therefore, they are responsible for building up body and hence rejuvenate and enhance vitality by enhancing disease resisting power of body [27]. Cell membrane protection, cell proliferation, self-renewal activity are some to define action of rasayana.
- *Nutraceutical Effect:* As rasayanas are rich in micro and macro nutrients, they help in promoting digestion at microcellular level by making optimal nutrition in dhatus and enhancing their microcirculation to effectively promote functional immunity and creating an environment where cells or tissues can grow smoothly and efficiently, regulating self-renewal progression, apoptosis and stimulating growth factors in order to sustain cellular homeostasis.
- *Radioprotective Action or Inhibition of Mutations:* The radioprotective components of rasayana medicine are phytochemicals that help in reducing biological effects of radiation by eliminating free radical species and repairing wear and tear caused by injuries from radiation [28]. Rasayana helps in detoxifying body by stimulating detoxification enzymes and inhibit activation of carcinogenic events.
- *Anti-Cancer Effect:* Cancer is abnormal growth of cells resulting in formation of aggregated mass of cells known as tumors. The anti-cancer ability of rasayanas is due to their immunostimulating property by increasing humoral immune response by forming anti-bodies forming cells and initiating their circulation in body. It has been found that rasayana administration has resulted in increased proliferation, cell migration, regulated apoptosis and reduction in tumor growth as well as in inhibiting spread of cancerous cells [29].
- *Anti-Inflammatory Effect:* Rasayana act as bio-substances that block certain substances in body that are subjects of causing inflammation (redness, swelling and pain). The phytochemicals of rasayana helps in blockage of inflammation starters by combining to the inflammatory receptor with phytochemical [24], thus occupying site of linkage and inhibiting inflammation pathway.

The benefits of Rasayana medicine could be achieved through described biological mechanisms but not limited to above mentioned effects. Action of Rasayana procedure results due to summation of multifactorial points working in synergy to improve dhatu nourishment at cellular level inside body [30]. Thus, significance of life depends on quality and quantity of nutrition it receives from rasayana.

CONCLUSION

The Rasayana therapy serves unimaginable and amazing results by promoting health, maintaining cellular level nourishment, strengthening body's immune defense, preventing onset of disease development as well as improving basic functions of body. This article demonstrates Rasayana, their classification based on various parameters, their phytoconstituents and possible biological mechanisms through activities of Rasayanas. Ayurveda's Rasayanas deals with every aspect of life from promoting health to laying foundation for cure of disease. Rasayana medicines as mentioned in Ayurvedic texts as well as proven studies helps in management of overall health of an individual by acting as immune-modulators, adaptogens, dealing with free radicals, nutritive, anti-inflammatory, anti-cancer, radio-protective, cyro-protective effects and many underline outcomes. Still there is insufficiency in fulfilling the gap between existing knowledge and the work that is needed to generate scientific evidence in support of mentioned benefits and actions of Rasayana medicine. Rasayana

being experience-based long tradition of use still apply in the era of modern science, therefore future research is encouraged in development of new strategies and pharmacological approach to reemerge rasayana as therapeutic drugs with scientific validation by coming generations of researchers.

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