



The Vayasthapan Karma (Age Sustaining Action) Of Haritaki (Terminalia Chebula Retz.)- A Review

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Abstract

Ageing is a natural ongoing process of unfavourable progressive changes correlated with deterioration in vitality and ending in death. *Haritaki* (*Terminalia chebula Retz.*) belonging to the family *Combretaceae* is the main herb used in *Ayurvedic* system of medicine since ages. The chapter 4 of *Charak Samhita Sutrasthan* deals with 50 different groups of 10 herbs with common action. The last of these groups is *Vayasthapan Mahakashay* i.e. the plants that prevent aging process and maintain the youth. One of the constituents of this group is *Abhaya* i.e. *Haritaki* which has an immense therapeutic significance. The plant is also documented to possess beneficial effects such as *Rasayana* (rejuvenating), *Medhya* (brain tonic) and *Deepan* (appetizer). It is very effective in the treatment of various ailments. By the virtues of *Agnideepan* (stimulating *Agni*), *Aampachan*(digesting *Aam*) and *Srotas-shodhana* i.e. cleaning the channels by detoxifying the metabolic waste, it supports the nourishment of *Dhatu*s and mind as well as boosts energy. It performs the functions of *Dhatwagnideepan* in addition to *Dhatwagniposhan* and helps to improve physical and mental health. It prevents degeneration, extends youth and delays aging or rather reverse the aging process. Following various claims for management of several diseases, efforts have been made by researchers to validate the efficiency of this plant regarding anti-aging potential through scientific biological screening. A analysis of literature in this regard exposed distinguished pharmacological activities of *Haritaki* like Anti-oxidant, Free radical-scavenging, Cyto-protective, Immuno-modulatory, Anti-mutagenic, Anti-carcinogenic, Radio-protective, Chemo-preventive, Chemo-modulatory, Cardio-protective, Hepato-protective, Nephro-protective, Adaptogenic, Anti-bacterial, Anti-amoebic, Anti-protozoal, Anti-fungal, Anti-viral, Anti-inflammatory and Anti-allergic activity. Its chemical investigation has also shown the presence of important medicinal virtues. The present attempt is to emphasize data about *Ayurvedic* aspect and phytochemical and relevant pharmacological study for justification of Anti-aging property of *Haritaki*. The interpretation of phyto-chemical and pharmacological study of this plant confirms the submissions made in the *Ayurvedic* classics about its *Vayasthapan* i.e. age sustaining action. The future research on the basis of this compiled information with the use of radiotracers and nuclear imaging techniques to know the action of this marvel drug at the molecular level can pinpoint unexplored potential of it for the treatment of degenerative disorders and give a key for the existing problem of premature aging.

Key words: *Vayasthapan, Mahakashay, Haritaki, anti-aging*

Introduction

Living long healthy youthful lifespan is a cherished wish of an every individual. Our natural health, happiness and internal sense of comfort are cloaked by the accumulation of impurities due to sedentary lifestyle, stressful mental conditions, excess use of pesticides, chemicals, preservatives and augmented use immunosuppressive drugs. These impurities or toxins lead to deterioration of normal body functioning and which affects the quality of life as well as lifespan. *Ayurveda* stands as an answer to solve this issue and provide healthful longevity including mental development and resistance against diseases. *Ayurveda* and other ancient Indian literature describe the use of plants in prevention and treatment of diseases of mankind since the time immemorial. Plants are used in traditional herbal medicines, which are being acknowledged in today's society as an important source of health due to their wide range of benefits including low cost of production, higher safety margins, non-toxic property and minimal risk of side effects.^{1,2} An inevitable physiological process in which the progressive losses of biological functions occur along with declining fertility and rising mortality with advancing age is called aging. *Ayurveda* mentions herbs that are believed to detoxify the body and mind; restore health; prevent degeneration and postpone aging or rather reverse the

aging process. And one of them is *Haritaki* (*Terminalia chebula* Retz., Family: *Combretaceae*) which possesses a great therapeutic value. It is used in traditional medicine due to the wide spectrum of pharmacological activities associated with the biological active chemicals present in this plant³. It is one of the constituents of numerous *Ayurvedic* formulations like *Triphala choorna*, *Abhayarishta*, *Pathyadi Kwath*, *Chitrakharitaki avleha*, *Agastiharitaki avleha* etc. which are used in day to day practise.

According to *Ayurveda* there are three parts of the lifespan of a person called as *Vaya*. They include *Balavastha* (childhood), which lasts up to the age of 16 years and *Kapha* is the predominant *Dosha* during this period which is responsible for growth and development; *Madhyavastha* (young and middle age), which lasts from the age of 16 years to 60–70 years and is governed by *Pitta Dosha* which is accountable for the vigour and vitality of youth.; and *Vridhdhavastha* or *Jirnavastha* (old age), which is the period after 60 or 70 years and *Vata* is the predominant *Dosha* during this phase of life and which is responsible for most of the manifestations of aging.^{4,5,6} This process of aging generally begins at the age of about 60 years and progress gradually and the effects are fairly noticeable at the age of 70 years.^{7,8} Natural Aging (*Kalaja*) occurs at or after the age i.e. 60 years but premature Aging (*Akalaja*) occurs before 60 years of age. The improper food and life habits lead to premature ageing. The process of aging leads to the progressive physiological changes in physical health such as deterioration in functions of body tissues (*Dhatu*), senses (*Indriya*), strength (*Bala*), virility (*Virya*), digestion and metabolism (*Agni*), and enthusiasm (*Utsaha*) together with wrinkled skin (*Vali*), grey hair (*Palitya*) and baldness (*Khalitya*); attack of various diseases like cough (*Kasa*), dyspnoea (*Shwas*), tremors (*Vepathu*) and unable to carry out work. The physiological changes in mental health comprise decline in mental functions like perception (*Grahana*), retention (*Dharana*), retrieval abilities (*Smarana*), speech (*Vachana*) and general knowledge (*Vigyana*)^{7,8}

According to modern scientist aging is unavoidable and every living organism has a finite life span. Ageing in individuals is affected to a greater extent by several factors like genetic factors, diet, social and environmental factors, the occurrence of age related disorders etc. Kanungo (1960) has described the causative factors of aging viz. Biological (decline of function of various organs), Medicinal (due to different types of diseases especially after 60 years) and Psychosocial. Biologically aging begins after the age of 21-22 years. After attainment of adulthood, the process of decline in functions of various organare begins. Fallia (1958) has explained Somatic mutation theory in late fifties⁹. Many theories have been stated related to ageing. Only a few could provide possible mechanisms of ageing. But, the most popular theory is 'Theory of free radicals' put forth by Dr. Denham Harmen which is still considered all over the world.¹⁰ According to Harmen D (1971)¹¹ and Pacific RE and Davis K J A (1991)¹² during biological reaction generally there is formation of free radicals like super oxide, hydroxyl ion etc. leading to progressive damage to macromolecules, protein and DNA and it is the primary cause of aging.^{11,12} For occurrence of lots of chronic and degenerative diseases like atherosclerosis, ischemic heart disease, cancer, diabetes mellitus, neurodegenerative diseases and ageing; oxidative stress caused by reactive oxygen species plays a vital role.¹³

The *Vayasthapan* drugs are those drugs which maintain the youth phase and hold-up the process of aging. *Aacharya Sushruta* mentions that *Rasayana* (rejuvenating) is *Vayasthapan* (sustains youth), gives long life, intellect and strength and also eliminates diseases.¹⁴ *Aacharya Gangadhar* states that *Vayasthapan* drugs stabilize youth, the supreme part of the age by their *Prabhav* (specific action of a drug).¹⁴ According to *Aacharya Dalhana* *Vayasthapan* drugs aid to live healthy life irrespective of its span¹⁴. In the chapter 4 of *Charak Samhita Sutrasthan*, *Aacharya Charak* has specified and described 50 *Mahakashay* with 10 herbal drugs in each group with common action to combat the particular disease or disorder or help contribute to positive health. Likewise there is a mention of the last group, named *Vayasthapan Mahakashay*¹⁵ i.e. group of herbs having age-sustaining action which include the plants like *Dhatri* (*Emblia officinalis* Gaertn), *Amrita* (*Tinospora cordifolia* (Willd) Miers ex Hook & Thems), *Atirasa* (*Asparagus racemosus* Willd), *Punarnava* (*Boerhaavia diffusa* Linn) etc. *Haritaki* (*Abhaya* i.e. *Terminalia chebula* Retz.) is the second plant of this group. It is a well known *Rasayana* which prevents aging and imparts longevity, immunity and body resistance against diseases. It is an endeavour on the part of this review paper to highlight not only an overall out line of *Haritaki* used in *Ayurvedic* drug scenario but also the recent as well as previously published information on phyto-chemical, toxicological and pharmacological actions of this amazing drug for validation of anti-aging property of *Haritaki*. The aim of this review is to promote further scientific researches to understand potential image of *Haritaki* as anti-aging drug because of its multi-dimensional therapeutic effect. The traditional knowledge with its unique and holistic approach supported by scientific experimental base can serve as an innovative and potent discovery engine for newer, safer drug.

The relevant data regarding *Haritaki's* Ayurvedic aspect from *Ayurvedic Samhitas* and *Nighantus* was obtained. Thorough review about the research work done by scholars on its phyto-chemical, toxicological and pharmacological actions were taken from various text-books, research journals and by surfing internet. All the compiled information was documented and critically analyzed for the discussion and attempt has been made to draw some fruitful conclusion.

Relevant Ayurvedic data

'*Abhayamalakiyarasayanapada*'¹⁶ is the very first quartet of first chapter of *Cikitsasthan* of *Carakasamhita* where the term *Abhaya* denotes *Haritaki*. In *Bhavprakash Nighantu* (*Ayurvedic material medica*) *Haritaki* is listed first because of its therapeutic significance. *T. chebula* is called as the 'King of Medicine' in Tibet.¹⁷

It has several common names such as Black Myrobalan, Ink tree or Chebulic Myrobalan (English), *Haritaki* (Sanskrit and Bengali), *Harad* (Hindi), *Harada* (Marathi and Gujarati), *Karkchettu* (Telugu) and *Kadukkaya* (Tamil). *Haritaki* denotes 'a fruit having dark greenish yellow colour, which drives away diseases' or it is sacred to God Siva (*Hara*). It is the best wholesome substance and safe for bodily passages (*Haritaki pathyanam*).¹⁸

Haritaki has several interesting synonyms like '*Pathya*'¹⁹ (it removes obstructions from the pathways and channels in the body); '*Abhaya*' (it gives fearlessness from diseases); '*Avyatha*' (it cures pain); '*Amruta*' (an ambrosia); '*Divya*' (a divine herb); '*Medhya*' (a brain tonic); '*Pranada*' (life saving); '*Jivanti*' (a vitalizing herb); '*Vayastha*' (it promotes longevity and maintains youth); '*Rasayanaphala*' (a rejuvenating fruit); *Kayastha* (which provides strength to body); *Putana* (eliminates waste); *Haimavati* (as its variety grows on Himalayas); *Chetaki* (helps to attain clear mind by cleansing channels); *Shreyasi* (takes care of the person who ingests it) and *Shiva* (provides all good things) etc. The mythological origin of the plant represents the immortal nature of therapeutic attributes in the human body.

T. chebula is a medium to large highly branched deciduous tree with a height up to 30 m and girth 1-1.5 m. It grows widely in India, Myanmar, Bangladesh, Iran, Egypt, Turkey, China etc. In India, it grows in deciduous forests of Himachal Pradesh, Tamil Nadu, Kerala, Karnataka, Uttar Pradesh, Andhra Pradesh and West Bengal²⁰ and it is found throughout India up to an altitude of 1500 m.²¹ The best variety of dried fruit of *Haritaki* has smooth texture and it is bulky, heavy, drowns in water and weighs approximately 20 grams equivalent to two *Karsha*. This *Haritaki viz. Survari Haritaki* is considered as excellent for medicinal usage²² and should be used for *Rasayana* (rejuvenating) and *Vayasthapan* (age-sustaining) purpose.

The fruits of tree possess diverse health benefits and have been used as traditional medicines as house hold remedy.^{23, 24, 25} It is used extensively in several *Ayurvedic* formulations prescribed for infectious diseases such as chronic ulcers, leucorrhoea, pyorrhoea and fungal infections of the skin. It is used as an ingredient of different formulations which are used in day to day practise for treating various disorders. It is used commonly in many *Ayurvedic* preparations as diuretic and cardiogenic.²⁶ It is used to prevent aging and impart longevity, immunity²⁷. According to *Aacharya Vagbhata*, when *Haritaki* powder fried in ghee is regularly consumed with sufficient ghee during meals, it promotes longevity and boosts energy. *Aacharya Bhavprakash* has mentioned its use in the treatment of lots of diseases like *Shwas* (Asthma), *Kasa* (Cough), *Prameha* (Diabetes), *Arsha* (Piles), *Kushtha* (Skin disorders), *Udar* (Ascitis), *Krimi* (Worms infestation), *Visarpa* (Herpes), *Jwara* (Fever), *Chhardi* (Vomiting), *Hridrog* (Cardiac diseases), *Kamala* (Jaundice), *Yakritvikar* (Liver disorders), *Ashmari* (Calculi) etc. He has also mentioned the beneficial effects of *Haritaki* on the health of eyes (*Chakshushya*), life (*Ayushya*) in addition to mental health (*Medhya*). Its *Rasayana* effect has been noted in many *Nighantus viz. Madanpal Nighantu, Raj Nighantu, Kaiyadev Nighantu, Bhavprakash Nighantu* and *Shaligram Nighantu*. For various medicinal purposes like laxative, carminative, astringent, expectorant and tonic effects, fruit of this herb is widely used in Thai traditional medicine.²⁸ It is routinely used as traditional medicine by tribes of Tamil Nadu to cure several ailments such as fever, cough, diarrhoea, gastroenteritis, skin diseases, candidiasis, urinary tract infection and wound infections²⁹.

Haritaki is extensively prescribed in therapeutic as well as preventive use and process of restorative indication (*Rasayana karma*), and in *Ayurvedic* classics description about *Ritu Haritaki* occurs which gives guidelines regarding use of this drug during the phase of different seasons along with specific Anupan (advantageous vehicle drug) viz., *Varsha Ritu* (Rains)- *Saindhavalavana* (Rock salt), *Sharad Ritu* (Autumn)- *Sarkara* (sugar), *Hemanta* (Cold/winter)- *Shunthi* (Dry Ginger), *Sishira* (late winter /early

spring)- *Pippali* (long pepper), *Vasanta* (Spring)- *Madhu* (honey) and *Grishma* (Summer)- *Guda* (Jaggery)³⁰.

The *Rasapanchaka* of *Haritaki* is as follows:

Rasa: *Kashay* (predominant), *Katu*, *Tikta*, *Amla*, *Madhura*

Virya: *Ushna*

Vipaka: *Madhur*

Guna: *Ruksha*, *Laghu*

Action on Doshas: *Tridoshashmaka* (pacify to all the *Doshas*)

Phytochemical properties

Haritaki is recognized to possess a wide range of phyto-chemical constituents. *T. chebula* have a number of phytoconstituents like tannins, flavonoids, sterols, amino acids, fructose, resin, fixed oils etc. and it is fairly loaded with different tannins (approximately 32% tannin content). The chebulic acid, chebulinic acid, chebulagic acid, gallic acid, corilagin and ellagic acid are the chief components of tannin.³¹ The studies showed that Phytochemicals such as anthraquinones, ethaedioic acid, sennoside, 4,2,4 chebulyl-d glucopyranose, terpinenes and terpinenols have also been present.^{20,32} Recent studies demonstrates that *T. chebula* contains more phenolics than any other plant.³³

Toxicological studies on *Haritaki*:

The herbs in the *Ayurvedic* materia medica have been established to be safe and effective, through many hundred to many thousand years of use.³⁴ The acute toxicity study of the 50% alcoholic extract³⁵, sub-chronic toxicity study of both powder and water extract³⁶, acute and chronic toxicity studies of water extract given orally³⁷ from dried fruits of *Haritaki* demonstrated no toxic effects in mice.

Pharmacological actions

1. Anti-oxidant and Free radical-scavenging activity

- *T. chebula* is an excellent anti-oxidant. It exhibited anti-lipid peroxidation, anti-superoxide radical formation and free radical-scavenging activities.^{38, 39, 40, 41} In a study, 6 extracts and 4 pure compounds of *T. chebula* exhibited anti-lipid peroxidation, anti-superoxide radical formation and free radical- scavenging activities at different magnitudes of potency³⁸ The ethanolic extract of the fruits of *T. chebula* decreased the level of lipid peroxidase in albino rats³⁹. Both treatment and pre-treatment of the cultured rat primary hepatocytes with *T. chebula* aqueous fruit extract (500 or 1000 mg/kg body weight for 5 days) significantly reversed the *t*-BHP-induced cell cyto-toxicity and lactate dehydrogenase leakage.
- In addition, *T. chebula* extract exhibited *in vitro* ferric-reducing anti-oxidant activity and 2,2-diphenyl-1-picrylhydrazyl free radical-scavenging activities. Histopathologic examination of the rat livers showed that *T. chebula* extract reduced the incidence of liver lesions including hepatocyte swelling and neutrophilic infiltration, and repaired necrosis induced by *t*-BHP⁴².
- *T. chebula* (aqueous extract) has strong anti-oxidant activity due to inhibition of radiation induced lipid peroxidation, which is observed in rat liver microsomes at different doses⁴².
- *T. chebula* (methanolic extract) found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals *in vitro*⁴³.
- Further, a hepato-protective compound, isolated from the ethanolic extract of the fruits of *T. chebula*, was identified as a mixture of chebulic acid and its minor isomer, neochebulic acid that also reduced the tert-butyl hydroperoxide (*t*-BHP)-induced cell cyto-toxicity in isolated rat hepatocyte experiment⁴³.
- *In vitro* evaluation of *T. chebula* shows that tri-ethyl chebulate is a strong anti-oxidant and free radical- scavenger, which might contribute to the anti-oxidative ability.⁴⁴ An aglycone isolated from the fruits of *T. chebula*, triethylchebulate, significantly inhibited FeSO₄ /Cys-induced microsomes lipid peroxidation and protected both H₂O₂-induced RBCs hemolysis and RBCs auto-hemolysis in a dose-dependent manner.
- Furthermore, triethylchebulate demonstrated potent DPPH free-radical-scavenging ability and moderately suppressed azide-induced mitochondria ROS formation. The results demonstrated that

triethylchebulate was a strong anti-oxidant and free radical-scavenger, which might contribute to the anti-oxidative ability of *T. chebula*⁴⁴.

- The aqueous extract of *T. chebula* seems to be able to protect cell organelles from radiotherapy-induced damages. The aqueous extract of *T. chebula* protected the anti-oxidant enzymes from reactive oxygen species (ROS) produced by gamma radiation in the rat liver microsomes and mitochondria.⁴⁵ *T. chebula* (Aqueous extract) exhibited xanthine/xanthine oxidase inhibition, 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals-scavenging activity.⁴⁵
- The leaves, bark and fruit of *T. chebula* demonstrated high anti-oxidant activity due to presence of phenolics.⁴⁶
- *T. chebula* (aqueous extract) inhibits free radical-induced hemolysis, nitric oxide release from lipopolysaccharide stimulated murine macrophages.⁴⁷
- *T. chebula* (Gallic acid and chebulagic acid, isolated from fruit extract) blocked cyto-toxic T lymphocyte (CTL)-mediated cyto-toxicity. Granule exocytosis in response to anti-CD3 stimulation was also blocked by the above phytochemicals at the equivalent concentrations.⁴⁸ *T. Chebula* (Acetone extract) has stronger anti-oxidant activity than alpha⁴⁸.
- *T. chebula* (ethanol extract) inhibited oxidative stress and the age-dependent shortening of the telomeric DNA length.⁴⁹
- *T. chebula* gall were tested for anti-oxidative and tyrosinase inhibition activities as well as for proliferative and MMP-2 inhibition activities on early aging human skin fibroblasts to evaluate *in vitro* anti-aging activity. The cold water extract of *T. chebula* gall indicated the highest stimulation index (SI) on normal human fibroblast proliferation. The extract also demonstrated MMP-2 inhibition on fibroblasts 1.37 times more potent than ascorbic acid. The study confirmed the traditional use of *T. chebula* gall in many Thai medicinal plant recipes for longevity.⁵⁰

2. Cyto-protective activity

- In the peroxidation model using *t*-butanol, *T. chebula* extract showed a notable cyto-protective effect on HEK-N/F cells. In addition, the *T. chebula* extract exhibited cyto-protective effect against UVB-induced oxidative damage. The life-span of the HEK-N/F cells was elongated by 40% as a result of the continuous administration of 3 µg/ml of *T. chebula* extract compared to controls.⁴⁹ The oxidative stress and inhibitory effect on cellular aging of its fruits have also been documented.⁴⁹
- Gallic acid and chebulagic acid, isolated from fruit extract of *T. chebula*, blocked cyto-toxic T lymphocyte (CTL)-mediated cyto-toxicity.^{48,51}
- It exhibited the development of duodenal ulcers and appeared to exert a cyto-protective effect on the gastric mucosa *in vivo*.⁵²
- *T. chebula* extract on the age dependent shortening of the telomere length as shown by the Southern Blots of the terminal restriction fragments of DNA extracted from sub-culture passages.⁵³

3. Immuno-modulatory activity

- Aqueous extract of *T. chebula* produced an increase in humoral antibody titer and delayed type hypersensitivity in mice.⁵⁴
- *T. chebula* found effective against the progression of advanced glycation end products-induced endothelia cell dysfunction.⁵⁵
- Crude extract of *T. chebula* stimulated cell mediated immune response in experimental amoebic liver abscess in golden hamsters.⁵⁶
- The formulation showed highest cure rate of 73% at 800 mg/kg body weight in hepatic amoebiasis. In immune-modulation studies, humoral immunity was improved where T-cell counts remained unaffected in the animals, but cell-mediated immune response was stimulated.⁵⁷

4. Anti-mutagenic and Anti-carcinogenic activities

- Crude extract of *T. chebula* fruit have chebulinic acid, tannic acid and ellagic acid, which are found to be the most growth inhibitory phenolics of *T. Chebula*.³³ The effect of 70% methanolic

fruit extract of *T. chebula* was investigated for growth of some malignant cell lines including a human (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and a non-tumorigenic, immortalized human prostate cell line (PNT1A) using assays for proliferation (3H-thymidine incorporation and coulter counting), cell viability (ATP determination) and cell death (flow cytometry and Hoechst DNA staining). In all cell lines revealed that the extract decreased cell viability, inhibited cell proliferation, and induced cell death in a dose dependent manner.³³

- Acetone extract of *T. chebula* has been reported to contain phytochemicals with promising anti-mutagenic and anti-carcinogenic properties.^{58,59}
- The chebulagic acid, one of the fractionated compounds from ethanolic fruit extract of *T. chebula*, showed potent dual inhibition against COX and 5-LOX. It also demonstrated anti-proliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145 and K562 cell lines.⁵⁹
- A recent study has shown the ability of Triphala to inhibit cytochrome P450.⁶⁰
- *T. chebula* (aqueous extract and hydrolyzable tannins) demonstrated Anti-mutagenic activity in *Salmonella typhimurium*.⁶¹

5. Radio-protective, Chemo-preventive and Chemo-modulatory activity

- In an experiment, aqueous extract of the fruit of *T. chebula* (50µg) was able to neutralize 1,1-diphenyl-2-picrylhydrazyl, a stable free radical by 92.9% and protected the plasmid DNA pBR322 from undergoing the radiation-induced strand breaks.⁴⁵
- *T. chebula* reduces irradiation effects in mice, human lymphocytes while undergoing the gamma radiation- *in vitro*^{62, 63} *T. chebula* extract in dose of 80 mg/kg body weight prior to whole body irradiation of mice resulted in reduction of peroxidation of membrane lipids in the liver and decrease in radiation-induced damage to DNA.⁶²
- Treatment of mice with aqueous extract of Triphala in different doses consecutively for five days before irradiation delayed the onset of mortality and reduced the symptoms of radiation sickness compared to controls.^{62,64}
- *T. chebula* showed chemo-preventive effect on nickel chloride -induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats.⁶⁵ *T. chebula* extract could be used as therapeutic agent for cancer prevention as it blocked or suppressed the events associated with chemical carcinogenesis.⁶⁵

6. Cardio-protective activity

- Cardio-protective effect of ethanolic extract of *T. chebula* fruits (500 mg/kg body weight) was demonstrated in isoproterenol-induced myocardial damage in rats. It was reported that pre-treatment with *T. chebula* extract had cardio-protective effect due to the lysosomal membrane stabilization preventing myocardial necrosis and inhibition of alterations in the heart mitochondrial ultrastructure and function in the experimental rats.⁶⁶⁻⁷⁸
- Pericarp of *T. chebula* has also been shown cardio-protective activity in isolated frog heart model.⁶⁹

7. Hepato-protective activity

- Protective effects of an aqueous extract of *T. chebula* fruit on the tert-butyl hydroperoxide-induced oxidative injury was observed in cultured rat primary hepatocytes and rat liver.^{42,43} *T. chebula* fruits showed strong hepato-protective activity through anti-oxidant effect in isolated rat hepatocytes.⁴³
- The similar property of its 95% ethanolic extract was observed against anti-tuberculosis drugs *i.e.* Rifampicin, Isoniazid and Pyrazinamide (combination)-induced toxicity in sub-chronic model (12 weeks) due to its prominent anti-oxidative and membrane stabilizing activities.⁷⁹

8. Nephro-protective activity

- The chloroform extract of *T. chebula* seeds (100, 200 and 300 mg/kg body weight) produced dose-dependent reduction in blood glucose of streptozotocin-induced diabetic rats in both short term and long term study (300 mg/kg body weight for 8 weeks). Further, remarkable reno-protective activity was also observed in *T. chebula* treated rats. ^{80,81,82}
- Oral administration of ethanolic extract of fruits of *T. chebula* (200 mg/kg body weight for 30 days) reduced the levels of blood glucose and glycosylated hemoglobin in streptozotocin (STZ)-induced experimental diabetic rats. ⁸³
- In a similar study, aqueous extract of *T. chebula* (200 mg/kg body weight for two months) reduced the elevated blood glucose and increase in glycosylated hemoglobin. The same dose also showed a marked improvement in controlling the elevated blood lipids as well as decreased serum insulin levels. ⁸⁴
- The *in vitro* studies with pancreatic islets showed that the insulin release was nearly two times more than that in untreated diabetic animals. The treatment did not have any unfavourable effect on liver and kidney function tests. ⁸⁴
- The fruit extract of *T. chebula* is helpful to alleviate the cadmium-induced nephro-toxicity in rats. ⁸⁵

9. Adaptogenic activities

- *T. chebula* along with several other medicinal plants helps to resist against a number of stressors in different ways. ⁸⁶

10. Anti-bacterial activity

- *T. chebula* exhibited anti-bacterial activity against various Gram positive, Gram negative bacteria such as *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa* suggesting its broad spectrum anti-microbial activity. ⁸⁷⁻⁹³ Thus various extracts of *T. chebula* exhibit anti-bacterial activity against a number of bacterial species. ⁹⁴
- Another study revealed that gram positive organisms inhibited on larger extent as compare to gram negative organisms. ⁹⁵
- Two antibacterial compounds, gallic acid and ethyl ester against methicillin-resistant *Staphylococcus*, have been isolated from ethyl alcohol extract of fruits of *T. chebula*. ⁹⁶
- *T. chebula* is well effective against *Helicobacter pylori*, a bacterium responsible for gastritis, ulcer and stomach cancers. The ether, alcoholic and aqueous extracts of *T. chebula* were tested against *Helicobacter pylori*, but aqueous extract of the plant, at a concentration of 1-2.5 mg/ml, inhibited urease activity of *H. Pylori*. ⁸⁹
- In a study some biologically active components were isolated from butanol fraction of fruit extract of *T. chebula* and tested against six intestinal bacteria. The strong and moderate inhibitory activity was observed against *Clostridium perfringens* and *Escherichia coli* by Ethanedioic acid respectively, with no adverse effects on the growth of the four tested lactic acid-producing bacteria. The study demonstrated Ellagic acid's potent inhibitory effect against *C. perfringens* and *E. coli*, but little or no inhibition was seen for behenic acid, β -caryophyllene, eugenol, isoquercitrin, oleic acid, α -phellandrene, β -sitosterol, stearic acid, α -terpinene, terpinen-4-ol, terpinolene, or triacontanoic acid. ⁹⁷

11. Anti-amoebic and Anti-protozoal activity

- The drug formulation of *T. chebula* was investigated for anti-amoebic effect in experimental caecal amoebiasis in rats and result showed curative rate of 89% at 500 mg/kg body weight due varying degrees of inhibition of enzyme activities such as DNase, RNase, aldolase, alkaline phosphatase, acid phosphatase, α -amylase and protease in axenically cultured amoebae. ⁹⁸
- The acetone extract of *T. chebula* seeds showed anti-plasmodial activity against *Plasmodium falciparum*. ⁹⁹

- In another study, *T. chebula* was evaluated in experimental amoebic liver abscess in golden hamsters and in immune-modulation studies. The formulation had a maximum cure rate of 73% at 800 mg/kg body weight in hepatic amoebiasis.⁵⁶

12. Anti-fungal activity

- The anti-fungal activity an aqueous extract of *T. chebula* was observed against a number of dermatophytes and yeasts. It is effective against the pathogenic yeast *Candida albicans* and dermatophytes *Epidermophyton*, *Floccosum*, *Microsporium gypseum* and *Trichophyton rubrum*.^{100, 101, 102, 103}

13. Anti-viral activity

- Herpes simplex virus 1 (HSV-1) is the cause of lifelong latent infection of sensory neurons. Hot water extract of *T. chebula* showed anti-herpes simplex virus (HSV) activity *in vivo* and anti-cytomegalovirus (CMV) activity both *in vitro* and *in vivo* in a study.¹⁰⁴
- Ledretan-96 and each of its 23 individual components were tested on an epithelial tissue culture cell line for their protective activity against cyto-toxic effects caused by influenza A virus. Of the 23 components tested, only one component showed a significant protective effect when applied to the epithelial cells individually.¹⁰⁵
- *T. chebula* can also be used in sexually transmitted diseases and AIDS.¹⁰⁶ The extract of fruits of *T. chebula* showed inhibitory effects on human immunodeficiency virus-1 reverse transcriptase.¹⁰⁷ A study proved that *T. chebula* fruits contain four human HIV-type 1 integrase inhibitors such as gallic acid and three galloyl glucoses, and suggested that galloyl moiety had a major role for inhibition of the 3'-processing of HIV-1 integrase by these compounds.^{108, 109}
- The aqueous extract of *T. chebula* executed the most prominent Anti-HBV activity by decreasing the level of extracellular HBV virion DNA at concentration ranging from 64 to 128 µg.¹¹⁰
- Two hydrolyzable tannins, chebulagic acid and punicalagin, isolated from the dried fruits of *T. chebula* inhibited HSV-1 entry at non-cytotoxic doses in A549 human lung cells by preventing binding, penetration, and cell-to-cell spread, as well as secondary infection.^{111, 112}
- Recently, acetone extract of *T. chebula* has emerged as a new alternative to treat pandemic swine influenza A infection due to its low cost, easy preparation and potential effect.¹¹³

14. Anti-inflammatory activity

- Aqueous extract of dried fruit of *T. chebula* showed anti-inflammatory activity by inhibiting inducible nitric oxide synthesis.¹¹⁴ Chebulagic acid extracted from tender fruit of *T. chebula* significantly suppressed the onset and progression of collagen-induced arthritis in mice.
- *T. chebula* in a polyherbal formulation (Aller-7) exhibited anti-inflammatory effect against arthritis in rats.¹¹⁵

15. Anti-allergic activity

- *T. chebula*, ingredient of a polyherbal formulation (Aller-7), showed potent *in vitro* anti-allergic activity.¹¹⁶
- Hydro-ethanol extract of *T. chebula* exhibit anti-histamine and anti-spasmodic in guinea pig ileum. [93]
- Oral administration of an aqueous extract of fruit significantly suppressed histamine release from rat peritoneal mast cells¹¹⁷ and also significantly increased production of tumour necrosis factor (TNF) by anti-dinitrophenyl IgE.¹¹⁸

Discussion

The advance age leads to occurrence of functional and structural changes in nearly all organ systems which results in gradually loss of some of their attributes in human beings. *Vayasthapan* is a group of herbs which are immune-stimulants and able to lessen the virulence of ageing and help to get better quality of life. *Ayurveda* mentions ageing as *Jaivika Swabhava* (biological nature of the living being).¹¹⁹

Ayurvedic classics mention that the physical structure consists of seven *Dhatus* starting from *Rasa* (*Rasadi Dhatus*). The health of other successive *Dhatus* (tissues) of the body depends on the qualities of the '*Rasadhatu*'. As these *Dhatus* develop sequentially and nourish further *Dhatus*, the medicine that improves the quality of '*Rasa*' promotes or strengthens the health of all tissues of the body. *Rasayana* herbs act on the fundamental factors of the body viz. *Dhatus*, *Agni* and *Srotasas* and help to stabilize aging. Thus all the body tissues are well nourished by *Rasayana*. The *Rasayana* medicines cause enrichment of *Rasa* (essence), ensuring promotion of health and strength of the tissues. Thus *Rasayana* help regeneration, replenishment and revitalization of *Dhatus*. *Haritaki* possesses these *Rasayana* properties.

According to *Ayurveda Tridoshas* regulate all the metabolic processes in the human body and carry out their action through *Dhatus*. The equilibrium of *Doshas* keeps person healthy and the disturbance in the equilibrium of *Doshas* results in a diseased condition. Thus *Doshas*, maintain homeostasis (*Dhatusamyā*). *Vata Doshā* deals with *Karshana* i.e. all catabolic activities (tissue wear and tear) that takes place in the body, *Pitta Doshā* is responsible for *Pachana* i.e. the process of nutrients assimilation into tissues and *Kapha Doshā* deals with *Brihana* i.e. synthesis of newer tissues. *Agni* has a key role in bio-transformation and *Saptadhatwagni* are accountable for tissue metabolism. The hypo-functioning of *Agni* results in the formation of the toxic waste of metabolism known as *Aam* which causes obstruction of the *Srotasas* (channels of micro-circulation). For tissue perfusion clear *Srotasas* are required. The clear channels aid in *Dhatu-Poshana* (Tissue Nutrition) by nourishing *Dhatus* which ultimately lead to formation of excellence of tissues and boosts *Ojas* (immunity). Thus for proper Nutrition, unimpaired tissue perfusion is an essential thing and *Ojas* is required for healthy regeneration of tissues.

By *Rasayana* drugs one can attain superior quality *Dhatus* (body tissues). *Acharya Shushruta* defines *Rasayana Tantra* as the measure which delays the ageing process, increases intellect and strength, prolongs life and cures the disorders. *Acharya Sharangdhara* mentions that *Rasayana* is the means by which old age and diseases are averted. *Ayurvedic Samhita* and *Nighantu* states *Rasayana* action of *Haritaki*. According to *Ayurveda* the action of drugs is interpreted on the basis of properties (*Gunās*) and *Rasapanchaka* is an indicator of drug action. The *Rasapanchaka* of *Haritaki* are very useful for *Agnideepan* (stimulating *Agni*), *Amapachan* (digesting toxic waste of metabolism) and *Srotas-shodhana* (clearing the channels of micro-circulation), hence by means of these actions, it normalizes the functions of *Jatharagni* and thereby it regularizes digestion and tissue metabolism. As a result restoration of *Agni* at the *Dhatu* level (*Dhatwagni-deepan*), removal of excessive *Kleda* takes place which results in proper nourishment of *Dhatus* and production of excellence of *Dhatus*.

Role of *Rasapanchaka* can be explained as follows:

Rasa: Kashay, Tikta, Katu, Amla and Madhur

- *Haritaki* possesses predominant *Kashay Rasa*. *Kashay Rasa* is the known for its *Stambhana* (Astringent) action. But *Haritaki* is an exceptional drug for this act as it has got *Madhur Vipaka* and *Ushna Veerya* along with *Kashay Rasa* which conducts *Anuloman Karma* i.e. it digests, breaks the adhesions and removes wastes through lower route. *Vayu Mahabhoota* in *Kashay Rasa* absorbs *Kleda*.
- *Tikta* and *Katu Rasas* are *Srotas-shodhak* i.e. channel cleaning. Due to *Vayu* and *Agni* predominance, *Katu Rasa* absorbs the fluid and stimulates *Agni*, digests *Aam* and *vilayan* property of *Agni* helps to expel the obstructive material.
- *Tikta rasa* acts in likewise by absorbing the fluid and slimy material owing to *Vayu Mahabhoota* and thus vacating space on account of *Aakash Mahabhoota*. Because of *Sookshma Guna* it permeates even to minute channels, thus helping the drug to reach at cellular level and depleting the accumulated *Kleda*.
- *Amla Rasa* help to stimulate *Agni* and *Madhur Rasa* is vitaliser and tonic.
- *Haritaki* is devoid of *Lavan Rasa*. According to *Acharya Vagbhata*, excess consumption of *Lavana Rasa* causes wrinkled skin (*Vali*), grey hair (*Palitya*) and baldness (*Khalitya*) which is manifestations of aging.

Veerya: Ushna

- It is dominated by *Agni Mahabhoota*. The speciality of *Haritaki* is that it has *Ushna Veerya* instead of *Sheet Veerya* although it is having *Kashay Rasa*. It stimulates *Agni* consequently corrects the *Dhatvagnimandya* and improves digestion and metabolism. It opposes any increment of unwanted *Kapha* by the *vilayana* property and helps in *Srotas-shodhan*. It alleviates *Vata* which is the predominant *Dosha* in an old age. *Agni* is the part and parcel of all bio-transformations in the body. According to *Aacharya Charak*, any principle which is responsible for action is considered as *Veerya*. In his commentary *Aacharya Shivdasa* states that *Veerya* is the potency which is situated in a particular portion of the drug where the potency lies in concentrated form.¹²⁰ This opinion more or less synchronises with the modern concept of active chemical fractions of the drugs which are accountable for action.

Vipaka: Madhur

- *Vipaka* has got systemic effect after metabolism. *Haritaki* has *Madhur Vipaka* in the place of *Katu Vipaka*. Therefore predominance of *Prithvi* and *Jala Mahabhootas* cause alleviation of *Vata* and *Pitta* which prevents Catabolism.

Guna: Ruksha and Laghu

- These *Gunas* help *Rasas* and thereby potentiates their action by way of synergism. They absorb *Kleda* and regulate *Jatharagni*.

Thus by the virtue of *Deepan, Pachan and Srotas-shodhan Karma Haritaki* increases *Agni* at all levels and reduces *Aam*, clears the channels resulting in correction of *Dhatvagnimandya*. Thus the actions of *Dhatwagnideepan as well as Dhatuposhan(by Madhur Vipaka)* make *Haritaki* the extraordinary drug. Because of these actions, the nutrients / essence reaches the *Dhatus* traversing through the minutes *Srotasas*. It improves the nourishment to *Dhatus*, thereby improvement in the defence system, *Agnibala, Dehabala and Satvabala*. Its *Medhya* (brain tonic) activity helps to combat the mental health problems of aging like decline in perception (*Grahana*), retention (*Dharana*), retrieval abilities (*Smarana*) as it improves higher integrative brain functions like memory, learning, thinking, understanding. Thus *Haritaki* restores physical as well as mental health and helps to delay the ageing process by *Rasayana* effect. It is interesting to note that it possesses *Tridoshashamaka* activity *i.e.* it alleviates all the three *Doshas*. References related to *Rasayana* are available such as turning old subjects to young, delaying the ageing process, prolonging the lifespan and increasing the strength of the individuals.¹²¹ *Aacharya Sharangdhara* has clearly mentioned that *Rasayana* are certain *dravyas* like *Rudanti, Guggulu, Haritaki* etc. which prevent early aging (*Jara*) and also guard against diseases or opportunistic infections.¹²² The same kind of description occurs in *Bhaishjyaranavali*.¹²³

Some of the causes of aging are unavoidable such as ultraviolet radiation, free radicals and genetic effects, social, environmental and behavioural influences. Free radicals are highly reactive and can cause great damage to the cell. They are able to attack healthy cells of the body leading them to lose their structure and the function. It appears to be the most important contribution to ageing and degenerative disorders in ageing. *Haritaki* has been investigated in terms of modern pharmacology for its Anti-oxidant, Free radical-scavenging, Cyto-protective, Immuno-modulatory, Anti-mutagenic, Anti-carcinogenic, Radio-protective, Chemo-preventive, Chemo-modulatory, Cardio-protective, Hepato-protective, Nephro-protective, Adaptogenic, Anti-bacterial, Anti-amoebic, Anti-protozoal, Anti-fungal, Anti-viral, Anti-inflammatory and Anti-allergic activity and observations of which overall indicate significant results of *Rasayana* and anti-ageing action. Apart from this there are several other therapeutic potentials of this wonder drug *T. chebula*.¹²⁴

Knowledge of the phytochemical constituent is very necessary to facilitate investigation of the actual effectiveness of the plant in medicine. The current research stress on health benefits of phytochemicals, especially anti-oxidant and anti-microbial properties of phenolic compounds, which exert protective activity against degenerative disorders, inflammation, allergies, infections by means of antioxidant, antimicrobial

and proteins/enzymes neutralization/modulation mechanisms. Phenolic compounds are reactive metabolites in a wide range of plant-derived foods and divided in four groups: phenolic acids, flavonoids, stilbenes and tannins. They work as terminators of free radicals and chelators of metal ions that are able to catalyze lipid oxidation.

Until now epidemiological knowledge bring to light that polyphenols show important functions such as inhibition of pathogens, anti-inflammation and anti-allergic activity, decompose microorganisms, prevent deposition of triglycerides, decrease the incidence of non-communicable diseases like diabetes, cancer, cardiovascular diseases and stroke which occur due to the factors like inflammation, allergy and reactive oxygen species. These protective effects are attributed, partially, to phenolic secondary metabolites.¹²⁵⁻¹²⁷

Polyphenols are considered to display their antioxidant capacity, depending on the hydroxylation status of their aromatic rings, including actions like scavenging of free radicals, chelation and stabilization of divalent cations, and modulation of endogenous anti-oxidant enzymes¹²⁸⁻¹³⁰

The anti-carcinogenic and anti-mutagenic potentials of tannins may be associated with their anti-oxidative property, which is important in preventing cellular oxidative damage, including lipid peroxidation. Tannins have also been reported to show other physiological effects, such as to reduce blood pressure, decrease the serum lipid level, modulate immunoresponses etc.^{131, 132}

Phenolic acids, hydrolysable tannins, and flavonoids have anti-carcinogenic and anti-mutagenic effects in view of the fact that they act as protective agents of DNA against free radicals, by inactivating carcinogens, inhibiting enzymes involved in pro-carcinogen activation and by activating of xenobiotics detoxification enzymes. In particular flavonoids and L-ascorbic acid have a synergistic protective effect towards oxidative damages of DNA in lymphocytes.¹³³⁻¹³⁵ High flavonoid intakes lead a decrease in LDL oxidation^{136, 137}.

Thus the above mentioned data shows therapeutic efficacy of *Haritaki* regarding anti-aging action which has been verified by using the modern pharmacological experimental models. The significance of *Haritaki* has been recognized and documented since ancient time due to virtue of its variety of chemical compounds, which possess important medicinal properties that can be used to cure diverse diseases. Therefore use of *Haritaki* promotes a youthful state of physical and mental health, postpones aging and expands happiness.

Conclusion

It is an attempt to emphasize the *Vayasthapan* action of *Haritaki* on the basis of *Ayurvedic* as well as modern scientific aspect The *Rasapanchaka* of *Haritaki* help it to conduct *Agnideepan*, *Aampachan* and *srotas-shodhana* actions i.e. it stimulates *Agni*, digests *Aam* and cleans the channels by detoxifying the metabolic waste and supports the nourishment of *Dhatu*s moreover mind and makes the body more energetic. *Haritaki* performs the functions of *Dhatwagnideepan* as well as *Dhatwagniposhan* and improves physical along with mental health. Consequently it guards against degeneration, prolong youth and delays aging. The observations of phyto-chemical and pharmacological study of this plant validate the submissions made in the *Ayurvedic* classics regarding its *Vayasthapan* i.e. age sustaining action. This herb merits advance research as it may be a source of potential anti-aging agent. In future study, the isolated principles from *Haritaki* needs to be evaluated in scientific manner by means of specific experimental animal models and clinical trials to know the molecular mechanism of action, in search of lead molecule from natural resources. This can open new avenue for the treatment of degenerative, autoimmune and metabolic diseases and provide a solution for the current issue of premature aging.

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