BIOCHEMISTRY AND PHYTOCHEMISTRY OF *TRIPHALA*, THREE MEDICINAL FRUITS, MEDICINAL PROPERTIES, BIOACTIVE COMPOUNDS AND THERAPEUTIC POTENTIAL

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Keywords: *Triphala*, Ayurvedic, Antioxidant, Gallic acid, Anti-cancerous, Hepatoprotective, Antidiabetic, *Emblica officinalis*, *Terminalia chebula, Terminalia bellirica*

Content

Summary

Triphala, is an Indian Ayurvedic formulation derived from dried fruits of three herbs, namely Amla (*Emblica officinalis*), Bahera (*Terminalia bellirica*) and Harar (*Terminalia chebula*) in equal proportions (1:1:1). The extract of mixture and its individual ingredients have high medicinal value as described in Ayurveda and showed many human physiological impact on body metabolism, digestion and nutrient absorption. *Triphala* powder contains good amount of important phytoconstituents having antioxidant properties and it is believed that these phytoconstituents are responsible for various therapeutic uses as well as pharmacological effects. It contains four major phenolics *i.e.* gallic acid, syringic acid, tannic acid and epicatechin along with ascorbic acid. *T. bellirica* contains stannic acid, gallic acid and ascorbic acid, while *T. chebula* contains gallic acid, syringic acid, tannic acid, ascorbic acid and epicatechin. Various research investigations have reported variation in concentrations of phytoconstituents among various brands of *Triphala* powder. It may be due to agro-climatic conditions, environmental conditions of storage, different sources of raw materials, different cultivars, and maturity conditions of fruits. Traditionally, Ayurvedic medicine '*Triphala*' has been used in problems related to digestion, poor food assimilation, colon cleansing and in chronic constipation. It possesses various pharmacological properties such as antioxidant, anti-cancerous, hepatoprotective, cardioprotective, hypocholesterolaemic, anti-aging, antidiabetic, antibacterial, antimutagenic, antiparasitic, antiviral, radio protective and many more. All these pharmacological properties of *Triphala* make it one of the most valuable household names and marketed herbal preparations in the Ayurvedic system.

1. Introduction

1.1. Constituents of *Triphala*

Plant kingdom has proved that it is an important source of pharmaceuticals which may be used in the treatment of many diseases (Vemuri et al., 2019). *Triphala* (Sanskrit; *tri* = three and *phala* = fruits) is an Indian Ayurvedic triherbal formulation, in an equi-proportional fruit mixture of three plant species *i.e.* Haritaki (*Terminalia chebula*), Bibhitaki (*Terminalia bellirica*) and Amalaki (*Emblica officinalis*) (Peterson et al., 2017; Tarasiuk et al., 2018; Figure 1). *Churna* means powder. It is also known as the 'three myrobalans'. Although, *Triphala* formulation is generally prepared with equal proportions of fruits from *T. chebula, T. bellirica*, and *E. officinalis* but a modified formulation of *Triphala* is also therapeutically used in the ratio 1:2:4 (Nariya et al., 2009). *Triphala* is an ayurvedic medicinal herbal formulation and has active phytochemical components which are responsible for its various pharmacological activities (Kumar et al., 2017). In ancient literature, Charaka Samhita explored that daily intake of *Triphala* Rasayana (*Triphala* alongwith honey and ghee) has the potential to make a person live for more than one hundred years and devoid of diseases (Agnivesa et al., 1976).

The use of natural formulations as medicine is gaining popularity due to its fewer adverse effects (Singh et al., 2014). Natural herbal formulations have been found to be safer medicines as compared to chemical drugs. According to Bulletin of World Health Organization (WHO), around 80% of the world's population relies on medicinal plants as their primary healthcare source (Sandhya et al., 2006). It has been assumed that about 50% of current medicines are developed from natural products and their derivatives, or their analogs (Newman and Cragg, 2007; Pan et al., 2013). Among them, cardiotonics (digoxin), anticancer drugs (paclitaxel and vinca alkaloids) analgesics (morphine), and the antimalarials (quinine and artemisinin) are modern medicines which have been isolated from plant systems (Poojary et al., 2015). *Triphala* is a familiar ayurvedic formulation in India, commonly prescribed by most ayurvedic healthcare practitioners. It exhibits anti-viral, anti-bacterial, anti-fungal and anti-allergic properties (Parveen et al., 2018). Physician Sushrut indicated that *Triphala* is useful in treating ulcers and wounds (Bhishagratna, 1963; Peterson et al., 2017).

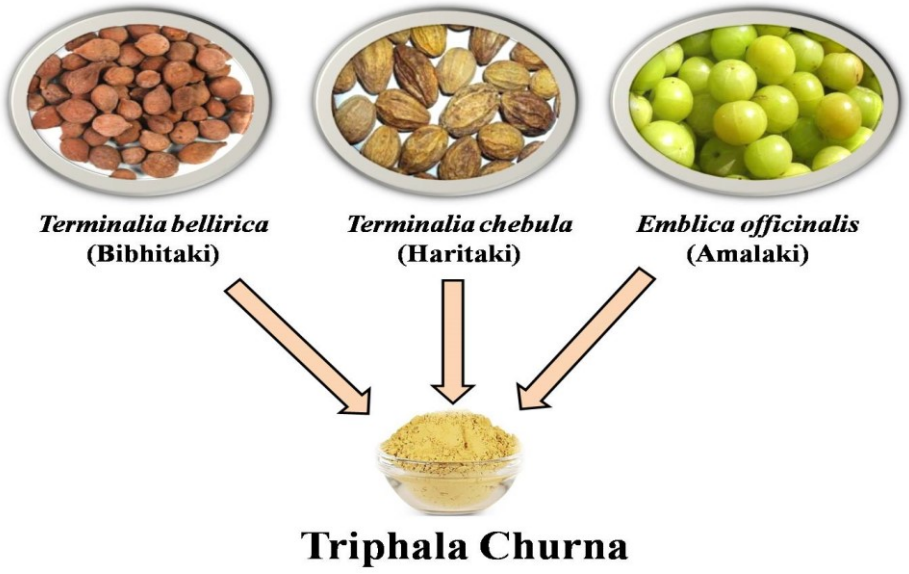

Figure 1. Constituents of *Triphala* Churna

1.1.1. *Emblica Officinalis* (Amalaki)

Emblica officinalis (EO), known as Indian Gooseberry or Amla in Hindi, has been used in Indian traditional system of medicine for thousands of years. *Emblica officinalis* was described by Joseph Gaertner in '*De Fructibus et Seminibus Plantarum*' in 1791 (Tropicos). Now it is known as *Phyllanthus emblica* L. (Figure 2). It is native to India, East Himalaya, West Himalaya, Bangladesh, Malaya, Cambodia, China South-Central, Pakistan, Thailand, China Southeast, Myanmar, Sri Lanka, Sumatera, Taiwan, and Vietnam.The fruit of this plant is of great medicinal value. It has a high content of Vitamin C. Extracts from various parts of *E. officinalis*, especially fruit, contain numerous phytoconstituents *i.e.* polyphenols like gallic acid, ellagic acid, quercetin, two major alkaloids (phyllantidine and phyllantine), astragalin-flavanol, emblicol, phyllembic acid, emblicanin-B, embicanin, different tannins, punigluconin-tanin, pedunculagin, terchebin, trigalloylglucose, corilagin, protein, carbohydrates, linoleic

acid, minerals, vitamins, amino acids etc (Variya et al., 2016; Narendra and Khurana, 2018).

It is used in fever, vomiting, indigestion, diarrhea, dysentery and haemorrhage. It has powerful antioxidant properties due to its high vitamin C content. It removes or neutralizes the excess free radicals generated due to oxidative stress and thereby reduces progression of degenerative diseases and ageing. Regular intake of *E. officinalis* also decreases serum glutamic-oxalacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT) and lactate dehydrogenase (LDH) levels in blood which indicate its cardio protective properties. *E. officinalis* has other wide number of pharmacological properties such as antidiabetic, antimicrobial, antimutagenic, anti-inflammatory, hepatoprotective, hypolipidemic, antitumor, gastro protective and chemo-protective.

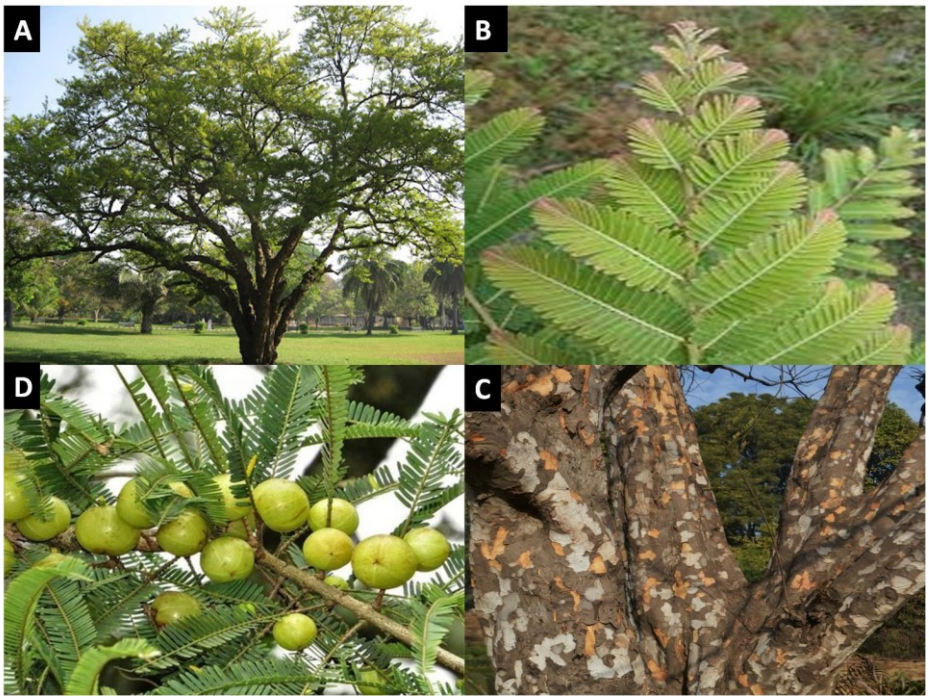

Figure 2. *Emblica officinalis* A. Plant B. Leaf C. Stem D. Fruit

1.1.2. *Terminalia Bellirica* (Bibhitaki)

Terminalia bellirica (TB) is known as Bibhitaki' in Sanskrit and "Bahera" in Hindi, is a large tree, up to 40 m high. *Terminalia bellirica* was first described as '*Myrobalanus bellirica'* by Joseph Gaertner in '*De Fructibus et Seminibus Plantarum'* in 1791 and later described taxonomically in its current nomenclature by William Roxburgh in '*Plants of the Coast of Coromandel*' in 1805 as *Terminalia bellirica* Roxb (Figure 3). Leaves are clustered towards the end of branches, and it is petiolate and broadly elliptic type. Flowers are solitary, simple, axillary and greenish-yellow in color. It is native to Bangladesh, Borneo, Cambodia, China South-Central, East Himalaya, India, Jawa, Lesser Sunda Island, Maluku, Myanmar, Nepal, Pakistan, Sri Lanka, Sulawesi, Sumatera, Thailand and Vietnam. In India, the distribution of *T. bellirica* is found in deciduous forests throughout the greater part of India, in the upper Gangetic plains,

Nagpur, Bihar, Orissa, West Bengal, Konkan, Deccan and most of South India (Hazra, 2019).

Fruits mainly contain chebulagic acid, gallic acid, ellagic acid, hexahydroxydiphenic acid, galloyl glucose, β‑sitosterol, ethyl gallate, methyl ester, mannitol, glucose, galactose, and rhamnose. The ripe dry fruit of *T. bellirica,* which is known as Belleric Myrobalan, is astringent, bitter, tonic and laxative. It is given in piles, dropsy, diarrhea, leprosy, biliousness, dyspepsia and headache. *T. bellirica* fruit extract shows antidiabetic, hepato-protective, antimutagenic, hypolipidemic, antimicrobial, antiviral, antimalarial, anti-HIV, antifungal, anti-mutagenic activities and lowers down the risk associated with atherosclerosis. Different parts of *Terminalia bellirica* are used in the treatment of wound healing, reducing fever, cough, diarrhea, skin diseases, oral thrush, laxation and in purification and circulation of blood in the body. Ethanolic leaf extract of *T. bellirica* exhibited strong antioxidant activity *in vitro* by chelation to metal ions as well as scavenging free radicals (Singh et al., 2012).

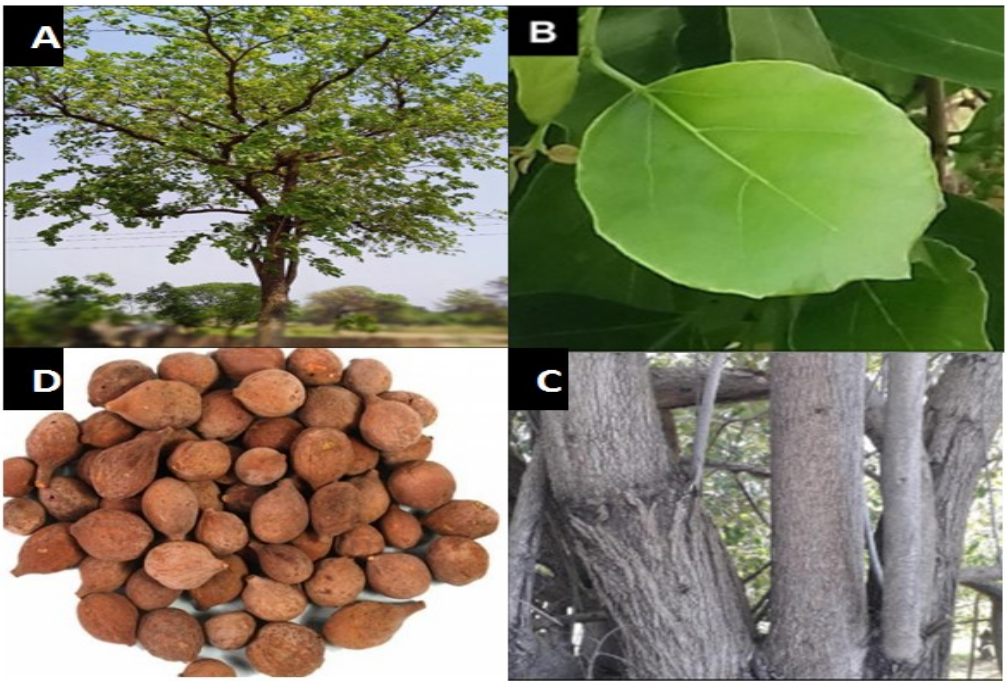

Figure 3. *Terminalia bellirica* A. Plant B. Leaf C. Stem D. Fruit

1.1.3. *Terminalia chebula* (Haritaki)

Terminalia chebula (TC) is the main ingredient in the Ayurvedic formulation *Triphala*, which is used to treat various dysfunctions. *T. chebula* has been extensively used in Ayurveda, Unani and Homoeopathic medicines and is known as “king” of Mongolian and Tibetan medicines (Zhang et al., 2018). *Terminalia chebula* was described by Anders Jahan Retzius in ‘*Observationes Botanicae*’ in 1789 (Figure 4). It is native to Bangladesh, Cambodia, China South-Central, East Himalaya, India, Laos, Myanmar, Nepal, Pakistan, Sri Lanka, Thailand and Vietnam. *T. chebula* tree commonly found in Northern India and also in South India at 1,000-3000 feet and up to 6000 feet in Travancore; higher forests of the Mumbai Ghats, Satpuras, Belgaum and Kanara (Mokat

et al., 2011). *T. chebula* is a deciduous tree growing up to 30 m height with a trunk diameter up to 1 m. Leaves alternate or opposite, thin-coriaceous, ovate or elliptic-obovate, with 2 glands at the base of leaf blade. Flowers white to yellow, monoecious, have a strong, unpleasant odour. Fruits are smooth, drupe-like, and yellow to orange in colour.

The most important product of this tree is the dried fruit which constitutes the black myrobalan of commerce, one of the most valuable Indian tanning materials. *T. chebula* exhibits a number of pharmacological properties due to the presence of a large number of phytoconstituents having antioxidant properties. A number of glycosides are present in *T. chebula*, including chebulosides I and II, arjungenin, arjunglucoside I and triterpenes. Plant extract contains alkaloids, flavonoids, phenols, carbohydrates, glycosides, terpenoids, saponins, proteins, and tannins (Pourmorad et al., 2006; Vemuri et al., 2019). Apart from this, other components include a coumarin connected with gallic acids called chebulin, chebulinic acid, ellagic acid, gallic acid, ethyl gallate, punicalagin, terflavin A, terchebin, 2,4-chebulyl-β-D-glucopyranose, luteolin and tannic acid. In addition, *T. chebula* also contains terflavin B, a type of tannin.

The fruit of *T. chebula* is an efficacious laxative, stomachic and tonic. The fruit pulp is given in chronic diarrhoea, dysentery, asthma, urinary disorders, vomiting, enlarged spleen and liver. It is used externally in wound healing and application to chronic ulcer. Modern pharmacological studies showed that it has many biological activities, including antimicrobial, anti-inflammatory, anti-oxidation as well as antitumor properties (Zhang et al., 2016).

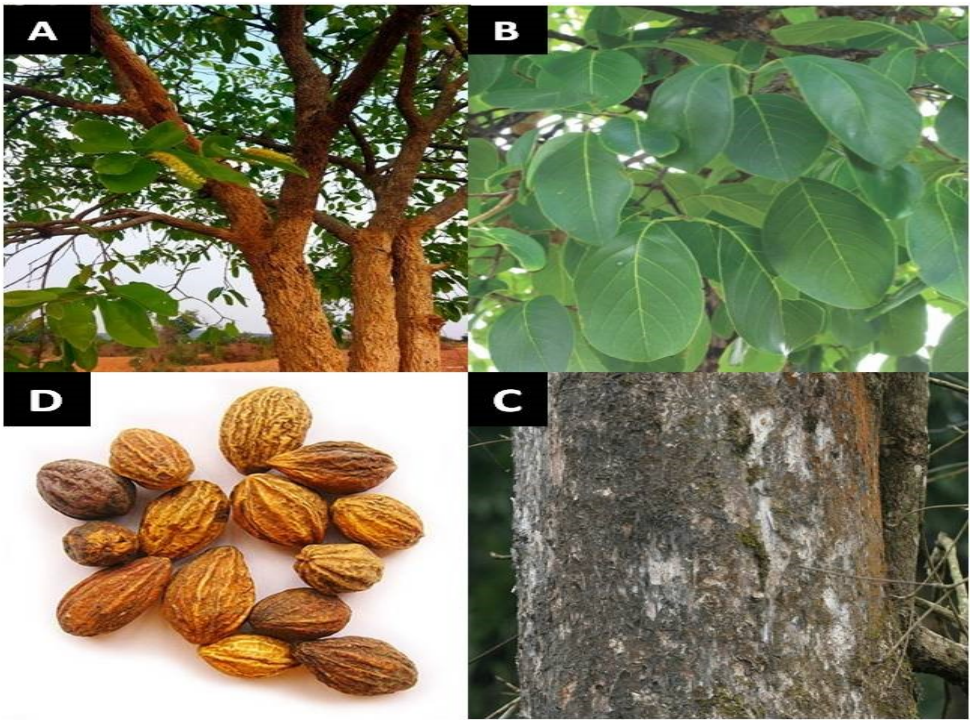

Figure 4. *Terminalia chebula* A. Plant B. Leaf C. Stem D. Fruit

1.2. Different Commercial Brands of *Triphala*

Triphala Churna can be purchased at health food stores, medical stores or online. A number of brands of *Triphala* are available in the market. It is available in many forms, including capsule, powder or liquid under different brand names such as Patanjali *Triphala* Churna, Baidyanath *Triphala* Juice, Dabur *Triphala* Churna, Arogyapath *Triphala* Powder, Healthvit *Triphala* Powder, Kapiva *Triphala* Juice, Banyan Botanicals *Triphala*, Toniiq *Triphala*, Organic India *Triphala*, Veda Organic *Triphala*, BRI Nutrition *Triphala*, Jiva Botanicals *Triphala*, Gaia Herbs *Triphala*, Maharishi Ayurveda Organic *Triphala*, Planetary Herbals *Triphala*, Himalaya Organic *Triphala*, Terrasoul Superfoods Organic *Triphala*, Nature Bell *Triphala* etc. The variability in efficacy in different brands of *Triphala* depends on several factors such as source of herbs collection, methods of processing, bioavailability, digestion, and absorption of herbal components due to inherent differences in gut microbiota that catalyze the biotransformation of the various *Triphala* components. It is suggested to take *Triphala* between meals on an empty stomach for maximum absorption and recommended doses range from 500 mg to one gram per day. *Triphala* Churna can be taken alone or in various combinations like mixed with warm water and honey, mixed with ghee, with honey and ghee, decoction, black ash, sugar etc. in the treatment of various disorders (Figure 5).

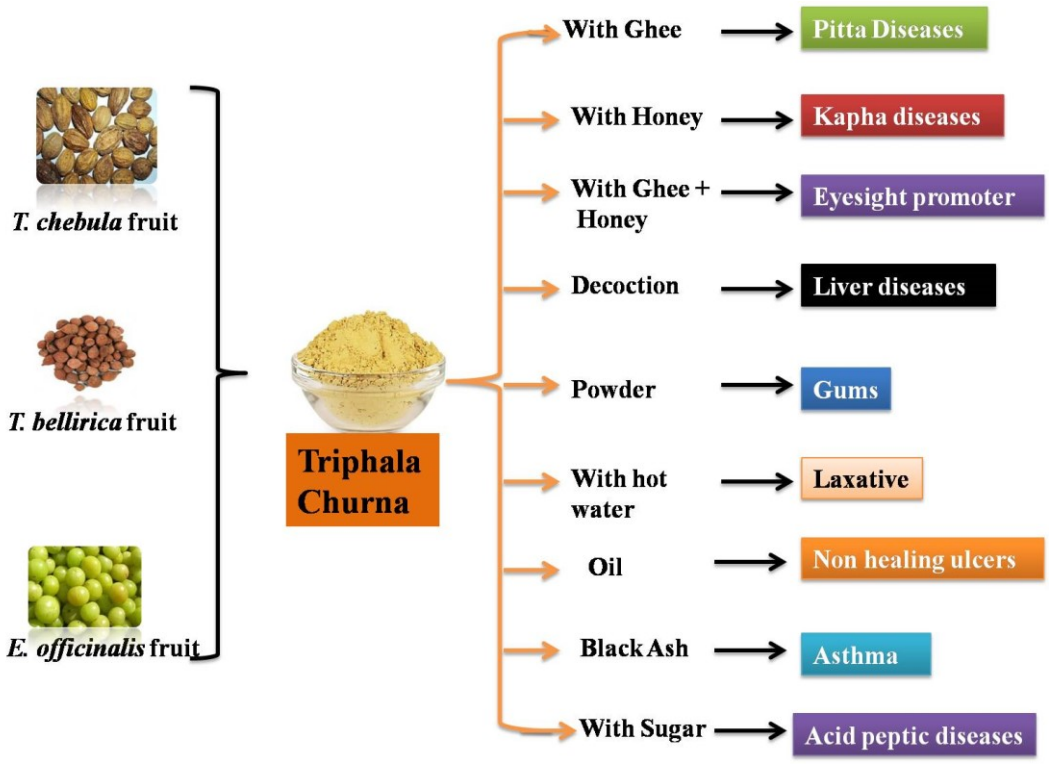

Figure 5. Combinations of *Triphala* Churna used in the treatment of various diseases

Significant improvements in the processing of crude plant materials have raised popularity of herbal remedies such as *Triphala*, which maximize the absorption of constituents; otherwise these components are poorly absorbed in the intestine. Despite

these improvements, these preparations still show pronounced variability in efficacy. This efficacy fluctuation is not recognized to spices and it may be due to phytochemicals ingested by people (e.g., plants-derived polyphenolic compounds). These characteristics must be present for true effectiveness of herbal remedies. It relates to the upkeep of human wellbeing and/or capability to reverse chronic disease states. For example, *Triphala*-derived polyphenols like chebulinic acid are transformed by the human gut microbiota into metabolites such as urolithins, which have the potential to prevent oxidative damage (Olennikov et al., 2015). The bioactivity of *Triphala* is induced by the gut microbiome to supply a widened spectrum and abundance of anti-inflammatory compounds. Reports also showed that co-administration of specific probiotic species with *Triphala*, enhanced absorption of phytocompounds in both the elderly and persons of all ages (Peterson et al., 2017). Thus, probiotic formulations comprising of bacterial species will be effective methods for improved digestion, bioabsorption and bioactivity of *Triphala*.

2. Bioactive Phytochemicals of *Triphala*

Chemical analysis of *Triphala* Churna revealed that it has high content of gallic acid, vitamin C, ellagic acid, chebulic acid, quercetin, luteolin, chebulinic acid, bellaricanin, β-sitosterol and flavonoids (Kumar et al., 2017) (Figure 6). Phenolic acids, flavonoids and tannins are the most commonly found polyphenolic compounds in plant extracts of *Triphala* (Naik et al., 2005; Sharma et al., 2014). Some of the important chemical compounds reported from this formulation are phenolics (25-38%), constitutes mostly of tannin (35%), gallic acid (3-7%), ellagic acid (2%), chebulagic and chebulinic acid (5%), epicatechin, syringic acid along with good amount of ascorbic acid (0.050-0.33%) flavonoids and saponin (Mukherjee et al., 2006; Naik et al., 2006; Sharma et al., 2012; Pharmacy et al., 2016). It also contains carbohydrates, steroids, tannins, terpenoids, alkaloids, flavonoids, cardiac glycosides, saponins, coumarins etc. *Triphala* also contains several other bioactive compounds such as flavonoids (luteolin and quercetin), anthraquinones, saponins, amino acids, fatty acids and various carbohydrates. Polyphenol chebulinic acid is also transformed by the gut microbiota into other bioactive metabolites, which have the potential to prevent oxidative damage (Olennikov et al., 2015). Major constituents are potent antioxidants that may account, at the minimum in part, for the observed immune-modulatory activity of the formula (Lee et al., 2005; Lu et al., 2012; Belapurkar et al., 2014).

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Pankaj Kumar Tripathi is presently working as a Postdoctoral fellow at Institute of Plant Sciences, Agricultural Research Organization (ARO), Volcani Center, Rishon Lezion, Israel. He did his M.Sc in Biotechnology with first class from Dr. Ram Manohar Lohia Avadh University, Ayodhya and obtained his Doctoral degree in Botany from Sikkim University, Gangtok, Sikkim. His doctorate research was focused on the area of Parkinson's disease (PD) and its management by L-Dopa, which is a precursor to dopamine and is considered as gold standard in the management of PD and dystonia. He has been in research profession since 2008. He did his post Ph.D job as a Scientist at Patanjali Research Institute, Haridwar and as a Project Coordinator in the Centre of Excellence at Indira Gandhi National Tribal University. Dr. Tripathi has published several research papers in journals of repute and presented his research papers in many National and International Conferences. He has also completed many national level projects funded by DBT, CSIR, DST and MoTA. He has interest in biodiversity, taxonomy, molecular biology, plant tissue culture, ethnomedcines/ traditional medicines, bioactive compounds, natural products, drug target & drug development, genetics & plant breeding.

Ram Lakhan Singh is presently holding the position of Vice-Chancellor of Nilamber-Pitamber University, Medininagar, Jharkhand, India. Professor Singh held the position of Professor of Biochemistry and Coordinator, Biotechnology Programme at Dr. Rammanohar Lohia Avadh University, Ayodhya, India prior to joining this assignment. He also held positions of Head, Departments of Biochemistry and Environmental Science; Dean, Faculty of Science; Dean, Students' Welfare and Director, Institute of Engineering & Technology in the same University. He has 34 years of experience as teacher, researcher and academic administrator. His main areas of research are Clinical/Nutraceutical Biochemistry, Environmental Biotechnology and Toxicology. He published 88 research papers in National and International journals of repute. Professor Singh has written/edited nine books published by Springer-Nature, Elsevier and CRC, and contributed 19 chapters in various books published by International publishers. He is on the panel of experts in academic bodies and selection committees of various universities/government organizations and funding agencies. He has been honoured as Best Teacher by International Association of Lions Clubs in 1999. Professor Singh has been awarded IUTOX Senior Fellowship by International Union of Toxicology during XI International Congress of Toxicology at Montreal, Canada in 2007. He has been conferred with 'Shikshak Shree Samman' by Government of Uttar Pradesh in 2012. Professor Singh has been admitted to the Fellowships of the Society of Toxicology, India in 2011 and Academy of Environmental Biology, India in 2015.