Chapter

Bioactive Phenolic Compounds from Indian Medicinal Plants for Pharmaceutical and Medical Aspects

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Abstract

Ayurveda is an age old system of medicine which utilizes thousands of medicinal plants, rich in secondary metabolites for their therapeutic benefits and phenolic compounds are important one. Plant phenolic compounds are one of the major group of phytomolecules having tremendous therapeutic and nutraceutical potential. Indian medicinal plants like *Emblica*, *Terminalia* spp., *Withania*, *Tinospora* etc. are some of the potential source of bioactive phenolics and had been used from ages in various *Ayurvedic* formulations and were scientifically validated too. In this contribution, a brief account of some common Indian medicinal plants rich in bioactive phenolics are summarized along with their therapeutic action on human health and disease. The vast array of phenolics in these plants makes them a suitable candidate for modern medicine, nutraceutical supplements, immuno-modulatory formulations etc. With the advent of modern separation tools and techniques, it is now possible to identify, isolate and purify desired phytoconstituents from plant extracts. This further opens the avenues of utilizing medicinal plants or plant constituents/metabolites as super food for strengthening the body and maintaining the healthy work-life balance. The need of the hour is to identify therapeutically potential phenolics rich plants and development of herbal formulations for human welfare.

Keywords: ayurveda, Indian System of Medicine, herbal drug market, bioactive phenolic compounds, herbal formulations, plant metabolites

1. Introduction

Secondary metabolites are the chemical compounds synthesized in plants having minor role in life processes and do not have direct role in normal metabolism and development of the plant but often have ecological roles e. g., attractants of pollinators and chemical defenses against microbes, insects and higher predators [1]. Several medicinal plants by virtue of their secondary metabolites acquire a number of biological and therapeutic activities. These phytochemicals influence the metabolic activities of human and animals and have been used as drugs since centuries. The secondary metabolites are classified in three chemically distinct groups- terpenes, phenolic compounds, and nitrogen containing compounds.

Phenolic compounds are a vast group of plant secondary metabolites, present in almost every plant in varying quantities. These are chemically heterogeneous and the derivatives include some very important compounds such as flavonoids, tannins, lignins, anthocyanins etc. [2]. They show huge diversity in the structure ranging from simple structures, e.g. phenolic acids, to polyphenol compounds such as flavonoids, which consist of several functional groups (**Figure 1**). Phenolic compounds are very crucial for the diverse therapeutic actions in medicinal plants, color and flavor of fruits etc. During food processing and storage, plant phenolics are converted to a variety of derived compounds. The flavonoids are the largest group of phenolic compounds and play major role in defense and pigmentation. These are reported to be synthesized in the case of occurrence of infection. The activities of different groups of flavonoids are different as per their structural class. These are more commonly known for their antioxidant potential by scavenging of free radicals mediated by the functional hydroxyl groups. Flavonoids are supposed to protect from infections, and also prevent from cardiovascular, cancer and age related problems [3]. This group of molecules are also responsible for the color, taste and fragrance to the flowers and fruits and in this way attract pollinators also.

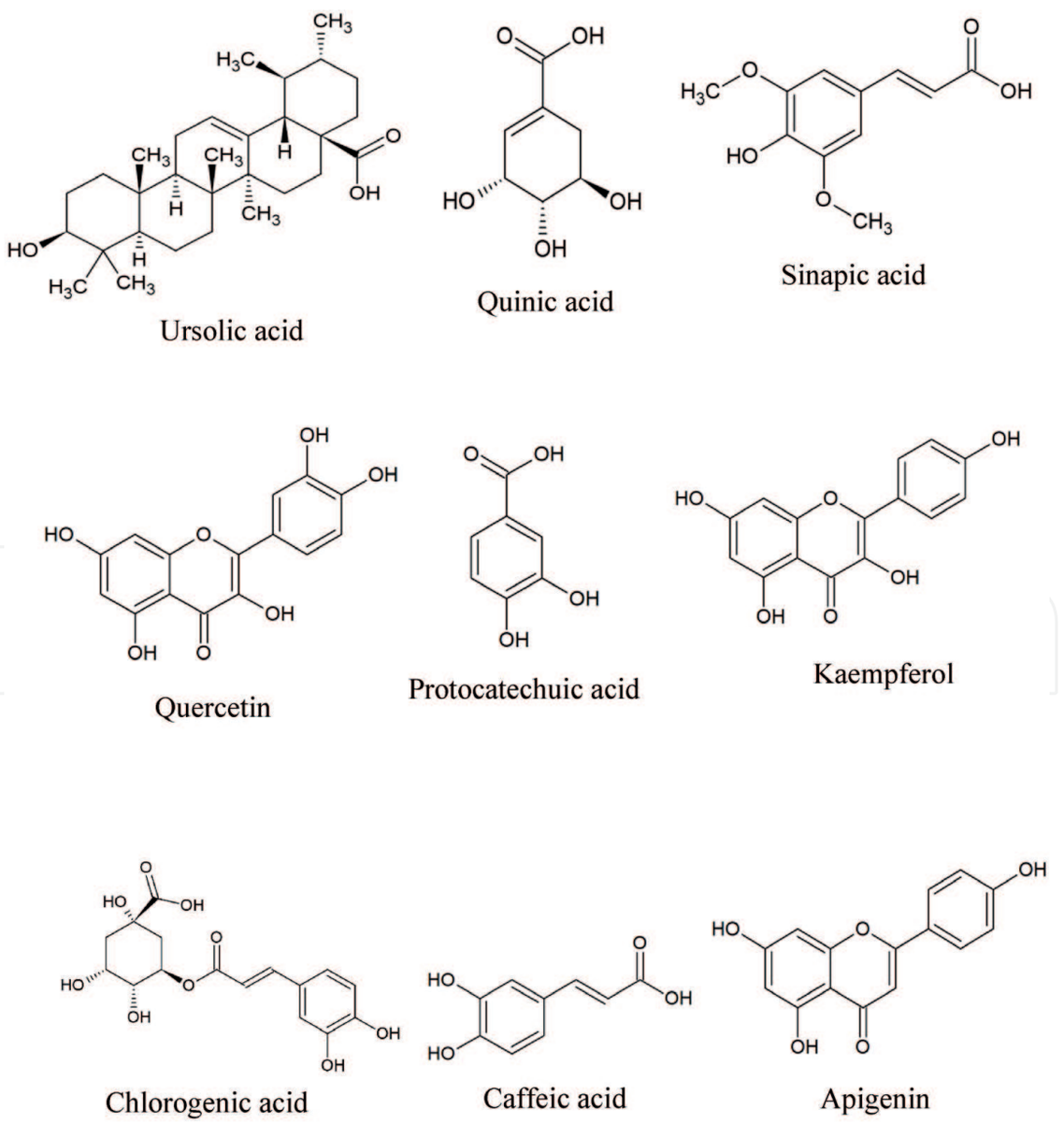

Figure 1.
Some common phenolic acids.

It is a well-established fact that the secondary metabolites in plants are meant to enable the plants to sustain their lives in various kinds of environmental conditions. Phenolic and flavonoid compounds are reported to exhibit strong antioxidant potential by different mechanisms. The hydroxyl group present in the phenolic compounds are excellent hydrogen donors. The reactive oxygen and nitrogen species react rapidly with hydrogen donating moieties which lead to stoppage of generation of new free radicals [4]. Phenolic compounds have also been found to chelate the metal ions involved in the formation of free radicals and hence produce antioxidant effect. Apart from antioxidant potential, dietary supplement of phenolic compounds have also been found to act as anticancer agents [5], provide protection from cardiovascular and several autoimmune diseases [6].

2. Traditional medicine and Indian Systems of Medicine (ISM)

The term "traditional medicine" (TM) refers to the ways of protecting and restoring health that existed before the arrival of modern medicine [7]. It incorporates plant, animal and mineral-based medicines, spiritual therapies and manual techniques designed to treat illness or maintain wellbeing [8, 9]. Many rural and ethnic communities in India use their indigenous knowledge for the treatment of various kinds of ailments [10]. They form the unwritten repository of health practices that have been verbally passed on to the next generations for at least one century and continue even today [11]. The World Health Organization (WHO) has also recognized the important role of traditional medicine in developing countries. WHO accepts that traditional medicine will continue to play an important part in providing services to very large number of people, particularly in rural areas [12].

India is a repository of vast traditional knowledge and a deep rooted system of indigenous medicine. According to a report from Government of India, about 75% of Indian population including majority of tribal and ethnic communities are mostly dependent on the traditional knowledge and practices for primary health care needs [13]. The system of medicines which are considered to be Indian in origin or the systems of medicine, which have come to India from outside and got assimilated in to Indian culture are known as Indian Systems of Medicine [14]. The age old Indian traditional medicine system "*Ayurveda*" is very extensive in terms of the plants used, owing to the great phytodiversity of the country. In addition, it is unique in having a well-defined conceptual framework which identifies it from many other traditional medicine systems [15]. In India, there are five recognized systems of medicine namely *Ayurveda, Yoga and naturopathy, Unani, Siddha and Homeopathy* (AYUSH).

The source of knowledge inculcated in *Ayurveda* finds its roots in one of the four ancient Indian texts (Veda), *Atharvaveda* which includes 114 hymns for prevention, treatment and cure of various diseases [14]. Two major written records of *Ayurveda* are *Charak Samhita* (for medicine) and *Shushrut Samhita* (for surgery). The fundamental principle of Ayurveda is to consider the physical and psychological status of body for maintaining healthy condition. It suggests ways to for proper life style and living in harmony with the nature. In Southern part of India, Siddha system of medicine is practiced. It has a close connection with the Tamil civilization and hence especially popular in Tamil Nadu. The experts of this medicine system are called *Siddhars* that means they have achieved excellence in this system of medicine. The siddha system of medicine uses drugs of metal and mineral origin to a large extent and with time it has included drugs of different other systems. The Siddha system resembles with Ayurveda as far as treatment procedures are concerned. The *Unani* system of medicine originated in Greece, established by Greek

philosopher Hippocrates. This system of medicine was introduced in India by the Arabs. Homeopathy was brought to India in the 18th Century, however, it has been very well received by Indians and made a part of Indian System of Medicine.

3. Medicinal plants: india's potential

India is one of the most diverse countries in the world having a rich repository of high value, endemic and rare medicinal plants [16]. In terms of plant diversity, India ranks tenth in the world and fourth in Asia [17]. The reason behind this vast diversity is the presence of different climatic conditions such as alpine in Himalayas to arid zones in Rajasthan. There are tropical forests in the Western Ghats while plateaus, mountains and valleys in North-Eastern states. Apart from varying topography, soil, rainfall, temperature, humidity conditions also differ from place to place which give rise to huge phytodiversity. The microclimatic variations further lead to differences in the phenology, metabolism, physiology, chemical profile and even morphology of plants in addition to growth pattern across the geography [18].

According to an estimate, more than 45,000 plant species are commonly found in India out of which flowering plants constitute around 15,000-18,000; members of bryophytes are around 1800; algal species are 2500; 1600 lichens; 23,000 fungal species exist in India [19, 20]. The surveys conducted by several workers have revealed that approximately 20,000 plant species are having one or the other medicinal properties [13, 21]. From Indian Himalayan Region (IHR) itself, 357 species of medicinal plants belonging to 237 genera and 98 families were recorded. Asteraceae, Lamiaceae, Rosaceae, and Ranunculaceae were the dominant families in the IHR region [22].

4. Market potential of herbal drugs

The use of herbal medicines has risen dramatically all over the world. Global sales of herbal products were anticipated to be US $ 60 billion in 2000 as per Secretariat of the Convention on Biological Diversity. The sale of herbal medicines is predicted to increase at an average annual growth rate of 6.4% [23]. In 2008, the global market for herbal remedies was about US $83 billion with a steady growth rate ranging between 3% and 12% per annum [24]. The market of herbal drugs has seen a good tendency of growth at a fast rate worldwide. There are several factors responsible for this growth like increased general awareness in people to protect from the side effects of synthetic medicine, more inclination of masses towards Ayurveda and herbal treatment; improvement in quality, proof of efficacy and safety of herbal medicines and high cost of synthetic medicines [25].

In India the medicinal plant market is mostly unorganized at present. Most of the herbal drug manufacturers procure the raw material from wild by overexploitation of available natural resources. Due to unavailability of sufficient quantity of raw material, adulteration of inferior quality raw material or similar looking plant species to the genuine drug is common practice in many of the herbal drug industries [26]. The value of medicinal plants related trade in India is US $ 5.5 billion, although its share in the global export market of herbal drugs is less than 0.5 per cent. The export potential of China in medicinal plants is nearly INR 18,000–22,000 Crores. India exports crude drugs mainly to developed countries like USA, Germany, France, Switzerland, UK and Japan. The principal Indian herbal drugs exported to foreign countries include *Aconite, Aloe, Belladonna, Acorus, Cinchona,*

Cassia tora, Dioscorea, Digitalis, Ephedra, Plantago and *Senna* etc. About 165 herbal drugs and there extract are exported from India [27].

5. Some examples of medicinal plants rich in phenolics

There are numerous Indian medicinal plants which are rich in bioactive secondary metabolites along with phenolic compounds. A glimpse of some of them are compiled in **Table 1**. A few plants rich in particular groups of phenolic acid are discussed below:

5.1 *Emblica officinalis* Gaertn. syn. *Phyllanthus emblica*

Emblica officinalis (fam.–Euphorbiaceae), commonly known as Indian gooseberry or *Amla,* is a very famous Ayurvedic medicinal plant highly rich in Vitamin C. It supports healthy metabolism, digestion, nourishes the heart and respiratory system, promotes healthy skin, eyes and hair, and builds immunity. It is a key ingredient of many well-known Ayurvedic formulations such as *Chyawanprah* and *Triphala* [54]. The fruits and leaves of Amla are highly rich in ascorbic acid, phenolic compounds, flavonoids, tannins etc. (**Figure 2**). Even the roots contain ellagic acid and lupeol [55]. The major phenolic compounds include gallic acid, quercetin, apigenin, ellagic acid, chebulinic acid etc. The phenolic content among the three ingredients of *Triphala* is highest in *E. officinalis* [56]. The fruit pulp is also rich in tannin content which gives it astringent properties [57]. The bioactive phenolic compounds impart several therapeutic effects to this plant such as anti-bacterial activity, anti-fungal activity, antioxidant and free radical scavenging activity, insecticidal activity, immunomodulatory activity, anti-inflammatory activity, anti-diabetic and hypoglycemic activity [58].

5.2 *Terminalia chebula* Retz

Terminalia chebula (fam.- Combretaceae), popularly known as *Harad*, is a widely used traditional medicine in Ayurvedic practice and the fruits are one of the ingredients of herbal formulation *Triphala*. It is a very well-known rejuvenating herb. In classical texts, it is reported as natural detoxifier, promotes bowel movement, improves digestion, anti-aging, and good for eyes. It has been suggested to take 1–3 grams of *Harad* fruit powder with a cup of hot water in case of irritable bowel disease associated with low digestion strength. The dried ripe fruit is used as a remedy for heart disorders, urinary disorders and asthma. Major phenolic compound present in *T. chebula* are chebulic acid, chebulagic acid, shikimic acid, ferulic acid, vanillic acid, p-coumaric acid, caffeic acid, gallic acid, ellagic acid, tannic acid (**Figure 3**) [59, 60]. Major flavonoids in *T. chebula* are rutin, quercetin, isoquercetin, luteolin, 3′-methoxyquercetin, pelargonidin [61–63]. It is also known for antioxidant, hepatoprotective, neuroprotective, cytotoxic, antidiabetic, anti-inflammatory activities among others [64]. The flavonoid content and antioxidant properties in *T. chebula* is greater than the rest of the two ingredients of *Triphala* and the order is *T. chebula* > *E. officinalis* > *T. belerica* [56].

5.3 *Terminalia bellirica* Roxb

Terminalia bellirica (fam.- Combretaceae), commonly known as *Beheda,* is another very crucial ingredient of *Triphala*. Its medicinal properties are well recognized across various traditional medicine systems and has been described in

Sl. No.	Plant name	Plant part	Major phenolic compounds reported	Ref.
1.	*Acorus calamus* Linn.	Rhizome	α-asarone and β-asarone	[28]
2.	*Achyranthes aspera* L.	Whole plant	Quinic acid, Shikimic acid, Gallic acid, Chlorogenic acid, Acetylsalicylic acid, quercetin, kaempferol	[29]
3.	*Aloe vera* (L.) Burm.f. (syn. *Aloe barbadensis* Mill.)	Fleshy leaves	Sinapic acid, Quercetin, Kaempferol, Apigenin, Gallic acid, Protocatechuic acid, Catechin, Vanillic acid, Epicatechin, Syringic acid, Chlorogenic acid, Gentisic acid, Caffeic acid, Coumaric acid, Ferulic acid, Rutin, Miricetin	[30]
4.	*Andrographis paniculata* (Burm.f.) Wallich ex Nees	Whole plant	Apigenin, Onisilin, Andrographidine C, Luteolin	[31]
5.	*Bacopa Monnieri* (L.) Pennel	Whole plant	Chlorogenic acid, neochlorogenic acid, caffeic acid, Apigenin, Quercetin, Ursolic acid, Luteolin	[32, 33]
6.	*Berberis aristata* DC.	Root	Anthocyanin, Rutin, Chlorogenic acid	[34, 35]
7.	*Biophytum sensitivum* DC.		Caffeic acid, Ferulic acid, Gallic acid, Chlorogenic acid, Rutin	[36]
8.	*Centella asiatica* (L.) Urban	Whole plant	Rutin, Quercetin, kaempferol, Chlorogenic acid	[37]
9.	*Costus speciosus* J. Koenig (Sm.)	Rhizome	Ferulic acid, Coumarin, Phloroglucinol, Orcinol, Catechin, Quercetin, Rutin, Luteolin, Kaemferol	[38, 39]
10.	*Cuculigo orchiodes* Gaert.	Rhizome	2,6-dimethoxy benzoic acid, curculigoside A, curculigoside B, curculigine A, curculigine D	[40]
11.	*Curcuma longa* Linn.	Rhizome	Curcumin, Demethoxycurcumin, Bisdemethoxycurcumin, Caffeic acid, Ferulic acid, o-Coumaric acid, p-Coumaric acid	[41, 42]
12.	*Datura metel* L.	Fruits	Gallic acid, Vanilic acid, Quercetin and Ferulic acid	[43, 44]
13.	*Diplocyclos palmatus* (L.) Jeffry	Fruits	Chlorogenic acid, gallic acid, caeffic acid and protocateuchic acid.	[45]
14.	*Elephantopus scaber*	Aerial part	Gallic acid, Proto catechuic acid Chlorogenic acid, Ferulic acid	[46]
15.	*Emblica officinalis* Gaertn.	Fruit	Ascorbic acid, Tannic acid, Gallic acid, Geraniin, Quercetin, Isocorilagin, Kaemferol	[47–49]
16.	*Gymnema sylvestre* R. Br.	Leaves	Epigallocatechin, Conduritol, Phloretin, Quercetin, Dihydroquercetin, Gingerol, Hesperetin, Myricetin, Orcinol, Phloretin, Rutin	[50]
17.	*Hedychium spicatum* Buch- Ham. Ex. Smith	Root	Chrysin, Teptochrysin, Ethyl cinnamate, Ethyl-*trans*-*p*-methoxy cinnamate, *p*-Methoxy cinnamic acid	[51–53]

Table 1.
Some Indian medicinal plants rich in phenolic acids.

Ayurveda, Unani, Siddha, as well as in traditional Chinese medicine. The fruits are useful in the treatment of asthma, bronchitis, hepatitis, diarrhea etc. [65]. Several phytomolecules from the phenolic class such as lignans, ellagic acid, gallic acid,

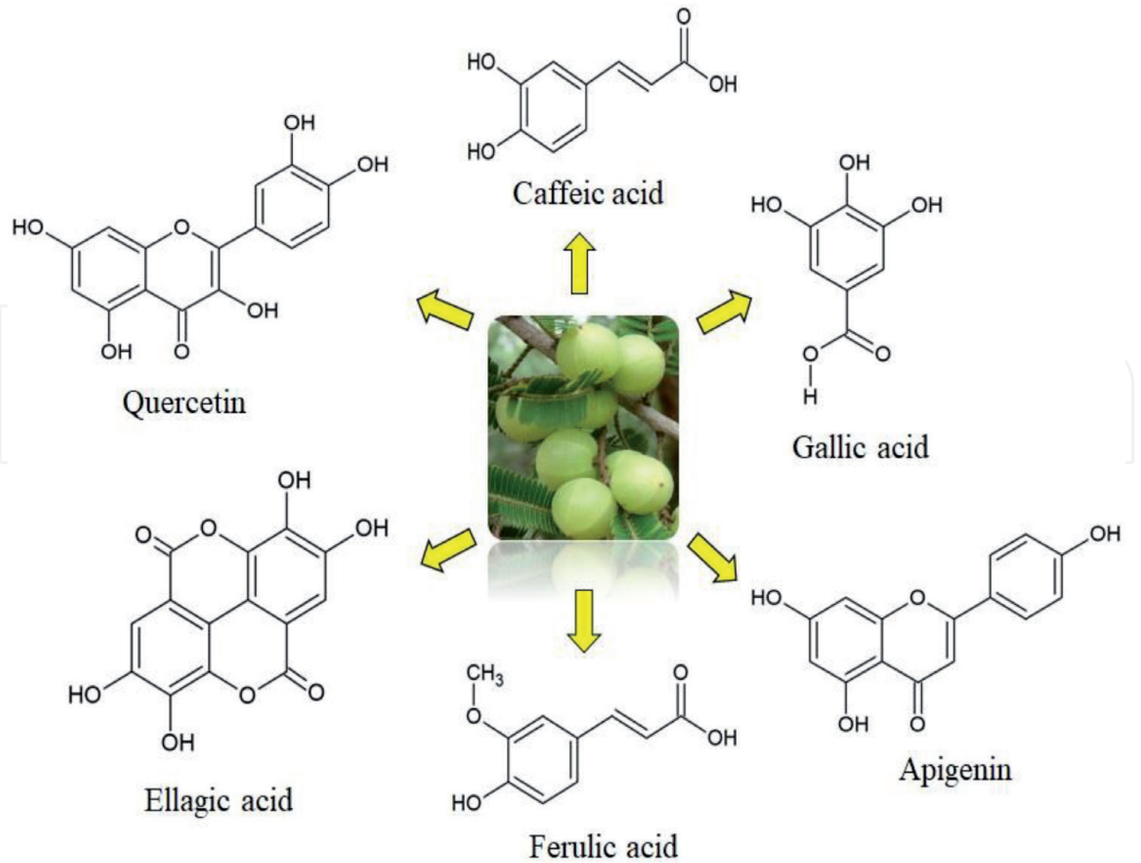

Figure 2.
Some phenolic acids found in Emblica officinalis.

chebulic acid, bellaric acid etc. has been found in the fruits of this plant [66, 67]. Ellagitannins such as corilagin, chebulagic acid, galloylpunicalagin, and digalloyl-hexahydroxydiphenoyl-hexoside were found to be the major components in *T. bellirica* [66].

5.4 *Tinospora cordifolia* (Thunb.) Miers

Tinospora cordifolia (fam.- Menispermaceae), commonly known as *Amrita,* is an age old Ayurvedic remedy for various purposes such as jaundice, diabetes, fever, skin diseases etc. It has been well known for scientifically proven roles as hepatoprotective, antipyretic, anti-oxidant, antimicrobial, anti-diabetic, immunomodulatory, anti-cancer etc. [68]. *T. cordifolia* is rich in many groups of phytomolecules such as alkaloids (berberine, tinosporin, palmetin, jatrorrhizine), terpenes, steroids, glycosides, saponins along with phenol and flavonoids. Major phenolic compounds reported are ellagic acid and kampferol [69].

5.5 *Tribulus terrestris* R. Br

Tribulus terrestris (fam.- Zygophyllaceae), also known as Gokshura is a well-known aphrodisiac in Ayurvedic and traditional Chinese medicine. It is highly rich in flavonoids and different flavonoids has been reported from different parts of the plant such as kaempferol, astragalin, quercetin and rutin from fruits and leaves [70, 71]. In a recent LC–MS study, identification of few phonic and flavonoid compounds has been done such as protocaatechuic acid, scopoletin, caffeic acid, quercetin, ferulic acid, rutin, luteolin, kaempferol, rutinoside etc. [72].

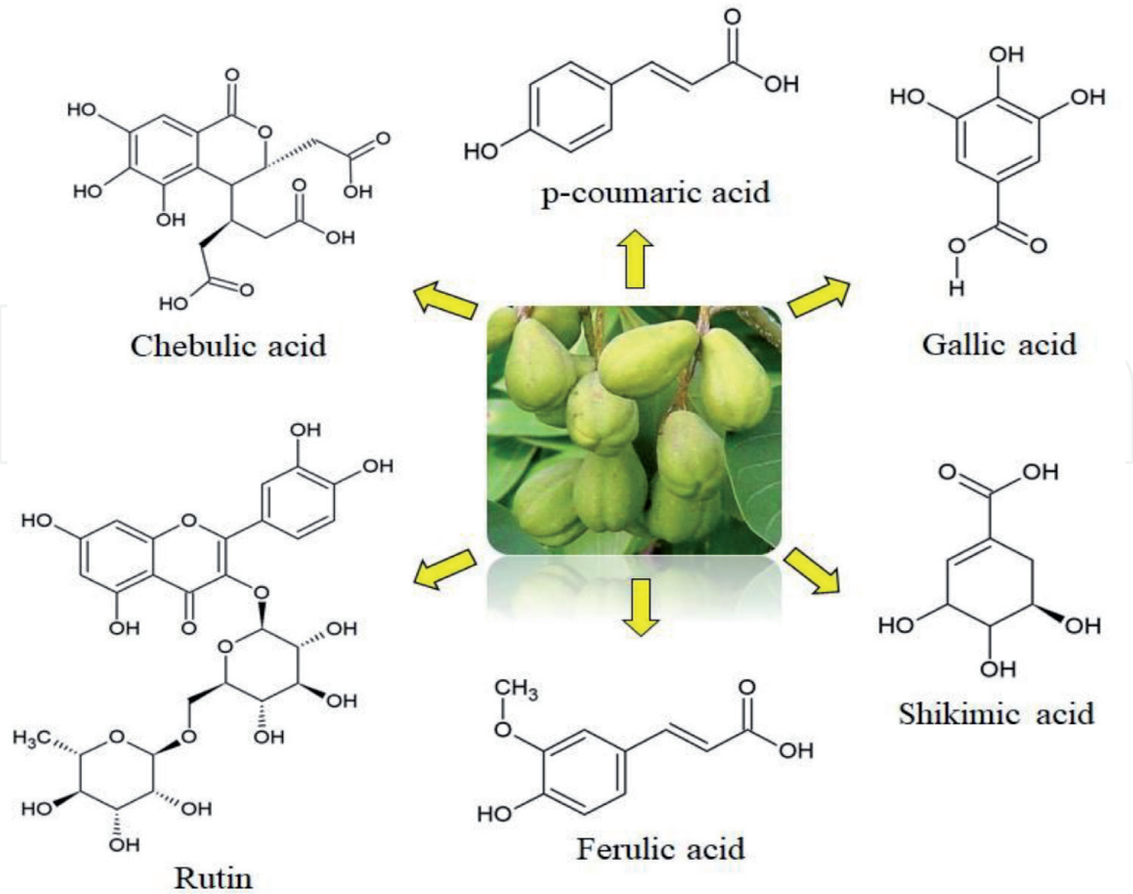

Figure 3.
Some phenolic acids found in Terminalia chebula.

5.6 *Withania somnifera* Dunal

Withania somnifera (fam.- Solanaceae), also known as *Ashwgandha*, is considered as a herbal tonic and health food in Ayurvedic texts and is considered as 'Indian Ginseng'. It is rich in many alkaloids such as withanolides and withaferin. Apart from alkaloids, *W. somnifera* is also rich in several phenolic acids and flavonoids, a few of which are catechin, gallic acid, syringic acid, vanillic acid, p-coumaric acid, benzoic acid, naringenin, and kaempferol [73].

6. Biological activities of plant phenolics and flavonoids

Plant phenolics and flavonoids possess a vast spectrum of biological activities ranging from general body maintenance to specific cure for many ailments such as cancer, diabetes etc. Many reports indicate that consumption of plant derived food material lowers the risk of many kind of diseases including cardiovascular diseases and cancer [74]. Their role as an anti-oxidant has been well established. There are different mechanisms for the anti-oxidant potential, however, radical scavenging via hydrogen atom donation is believed as the main mechanism [75]. The phenolic acids are also recognized as antidiabetic agents as they are able to influence the role of glucose and insulin receptors [76]. Few phenolic acids readily inhibit the activities of α-glucosidase and α-amylase which are responsible to convert dietary carbohydrates into glucose [77–79]. There are several reports showing role of phenolics in treatment of cancer through different mechanisms. Hydroxybenzoic and hydroxycinnamic acids are phenolic acids known for prevention and treatment of

cancer [80]. In conclusion, it can be said that these molecules are extremely useful in various beneficial roles for human health.

7. Conclusion

The Indian traditional system of medicine "*Ayurveda*" has rich heritage in mitigating the disease and discomfort of individual with the use of medicinal plants and/plant products. With the advancement in knowledge about plant sciences and sophisticated analytical techniques, the therapeutic potential of medicinal plants can be easily related to their bioactive metabolites. Among the various class of phytomolecules, phenolic compounds are the most abundant, naturally available secondary metabolites having therapeutic potential. Some potential Indian medicinal plants like *Withania somnifera, Tinospora cordifolia,* etc. have multifarious medicinal benefits, are being used from ages and their efficacy is well proven in recent times too. There are reports that suggest a higher intake of vegetables and fruits rich in phenol and flavonoids can lower the risk of diabetes and cardiovascular diseases. In a recent study, the importance of phenolic compounds and their significance in management of type 2 diabetes as well as in human nutrition has been done and found that the role of phenolic compounds are vital for anti-aging, anti-inflammatory and anti-oxidant properties [81].

Up to 19th century, the concept of using medicinal plants in diet is restricted and considered for patients only. However, in recent times the emergence of nutraceutical benefits of plant based products has brought the medicinal plants into our plates. Further, the need of functional foods, dietary supplements, and super foods like Kale, Spirulina, Chia seeds, omega-3 rich foods, *Moringa* leaf powder, has diverted the focus of society in using newer and alternate source of nutrition which can supplement the basic traditional food. Therefore, looking to the relevance, indeed there is need of incorporating medicinal plants rich in phenolics compounds into our daily diet for promoting health and wellbeing.

8. Future perspective

With a growing awareness about the benefits of herbal products across the globe, now a days there is huge demand of food supplements, nutraceuticals, health promoting herbal medicines etc. than ever before. Most of these supplements are rich in phenolic compounds that attribute anti-oxidant potential, health promoting effect, immunomodulatory potential, and maintain general health. More recently, the race of boosting one's immunity enlightens the world about using *Ayurvedic* medicinal plants as dietary supplements, in cohesion with guidelines of regulatory bodies. Keeping this scenario in mind, there is an opportunity for the scientific community to explore the potential of phenolics from medicinal plants with the advent of improved techniques of extraction and purification of phenolics. In a recent study, analysis of phenolic compounds in different parts of *Amaranthus cruentus* was done and found that the type and quantity of phenolic compounds varies across plant parts and also the harvesting time. The quantity of phenolic compounds was found higher in the tender and mature leaves and rutin was found as the most abundant compound in the vegetative part [82]. This kind of study can help us get the better quality and quantity of secondary metabolites from the plants which will be detrimental for developing an efficacious herbal product. The process further needs to be scaled up for their optimum industrial scale prospection for human welfare.

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