ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 9, Issue 5, 2016

Online - 2455-3891
Print - 0974-2441

Review Article

TERMINALIA CHEBULA: SUCCESS FROM BOTANY TO ALLOPATHIC AND AYURVEDIC PHARMACY

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Received: 25 May 2016, Revised and Accepted: 27 May 2016

ABSTRACT

Terminalia chebula (TC) is a unique herb having various therapeutic potentials as anti-inflammatory, antioxidant, anticancer, and digestant. It belongs to family Combretaceae. In the present review, an attempt has been made to decipher classification, chemical constituents, therapeutic uses, and patents that have been reported for TC. Various pharmacological activities of TC that make it as potential medicine and its Ayurvedic formulations are highlighted.

Keywords: *Terminalia chebula*, Anti-oxidant, Anti-cancer, Ayurvedic formulations, Anti-oxidant.

 DOI: http://dx.doi.org/10.22159/ajpcr.2016.v9i5.13074

INTRODUCTION

Terminalia chebula (TC) is a unique herb that is used from ancient time since Charak. It is used in many herbal formulations like Triphala. It is used as anti-inflammatory and digestant [1-3]. In recent years, an extract of TC has been reported for having anticancer and antioxidant properties [1-3]. TC belongs to Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Order: Myrtales, Family: Combretaceae, Genus: *Terminalia,* Species: *Chebula* Rtz [4,5].

It is known by different names in different languages such as Harad in Hindi, *Haritaki* in Sanskrit, *Chebulic myrobalan* in English, *Karakkaya* in Telugu, and in Tamil known as *Kadukkai*. Some other synonyms of *TC* are *Amrta, Abhaya, Kayastha, Vayastha, Pathya, Vijaya, Siva Jaya,* and *Haimavti*.

CATEGORIZATION OF TC AS PER AYURVEDA

TC has different varieties and the information of these varieties differ in Ayurvedic and modern text [6,7].

Categorization as per *Bhavamisra*

Acharya Bahvmishra mentioned about different varieties of *Haritaki* in his text. He explained about number of different varieties along with their uses are given below:

1. *Vijya* – used for *sarvarog* (all diseases)
2. *Rohini* – used as *varan* (bearing wound healing property)
3. *Putana* – used as *pralepa* (external applications)
4. *Amrta* – used for *shodhan* (purification procedures)
5. *Abhya* – used for *netrarog* (eye diseases)
6. *Jivani* – used for *sarvarog* (all diseases) [6].

Categorization as per Indian Materia Medica

Different varieties along their morphological characters and uses according to Indian Materia Medica are given below.

Survariharade

Large, dense and heavy size about 2″ long, yellowish to brownish in color, when cut it contains pulp of yellowish to brownish tinge. This variety is valuable purgative.

Rangariharade

These are smaller in size, less wrinkled, and less furrowed than *Survariharade* and its length is about one inch; when cut it presents a yellow dried pulp and stone. The pulp is also less astringent than above variety. These are alterative, stomachic, laxative, and tonic. It is generally used in fevers, cough, asthma, urinary diseases, piles, worms and rheumatism and scorpion-sting.

Balaharade

This variety is smaller than above two mentioned categories, its color is homogenous, and the pulp is deep brown. There is no stone into it. This is mild and safe aperients and antibilious, though astringent. Ripe fruits are considered as purgative removing bile and phlegm and to adjust bile. It is used in is highly useful in chronic diarrhea and dysentery, flatulence, vomiting, hiccups, colic and enlarged spleen and liver. Brayed with sugar and water it is used in ophthalmia.

Java harade

These are smallest than all of above varieties and rest characters are similar as that of *Balaharade*. The uses of this variety are similar as that of *Balaharade*. Along with that cold infusion of it is used as a gargle in sore mouth and stomatitis, spongy and ulcerated gums. Brayed in rose water it is a cooling application to swellings [8].

Categorization as per Hooker's flora of British India

In Hooker's flora of British India, apart from TC, six other varieties of TC are mentioned [9,10]:

TC Retz. (variety chebula proper)

Fruits, one-to one-and-a-half inches, ellipsoidal or obovoid, from a broad base, more or less glabrous, and five-ribbed are abundant in Northern India at 1000-3000 ft.

TC (var. typica)

They have a young ovary and are shaggy without calyx teeth. They are distributed in Deccan, Ceylon, and Burma.

TC (var. citrina)

They have a young ovary, are quite glabrous, with ovate fruit, and a round base. It is common in Northern India, from Kumaon to Bengal and in Chhota Nagpur.

TC (var.)

The fruits of this variety are much smaller than the other varieties. Generally found in Bihar up to an altitude of 1000 ft.

TC (var. tomentella, Kurz)

Young ovary, are glabrous, fruit is ovoid, and hardly one inch in diameter.

TC (var. gangetica Roxb.)

They have fruits with brown silky hair, which covers the twigs. It may be a very good variety. The fruit is similar to that of chebula, distributed in Northwest India.

TC (var. parviflora Thwaitos Enum.)

They have fruits that are more acutely ribbed [9,10].

Table 1 describes varieties of TC according to different ancient texts such as Raja Balabh Nighantu, Atreya Shamita, Harita Shmita, Saligram Nighantu, Raj Nighantu, Bhav Praksh Nighantu [11-13].

CHEMICAL CONSTITUENTS

TC mainly contains hydrolysable tannins as active constituent. Chebulinic acid (CA) is the main active constituent present in TC. Other constituents are chubulagic acid and D-galloyl glucose, free tannic acid, gallic acid, ellagic acid, and resin myrobalanin. Anthraquinone glycosides, sennosidesare also found in TC [1,3]. These tannins contain phenolic carboxylic acid like gallic acid, ellagic acid, chebulic acid, and gallotannins such as 1,6 di-*O*-galloyl-β-D-glucose, 3,4,6 tri-*O*-galloyl-β-D-glucose, 2,3,4,6 tetra-*O*-galloyl-β-D-glucose, and 1,2,3,4,6 penta-*O*galloyl- β-D-glucose. Ellagitannin such as punacalagin, casurarinin, corilagin, and terchebulin and others such as chebulanin, neochebulinic acid, chebulagic acid, and CA are also present in TC [1,3].

ISOLATION AND EXTRACTION OF ACTIVE CONSTITUENTS PRESENT IN TC

CA and chebulagic acid was extracted from TC by high-speed counter current chromatography method [3]. The solvent system used for this was n-hexane-ethyl acetate-methanol-water (1:20:1:20 v/v). The partition coefficient at this solvent system for chebulagic acid was 0.65 and CA was 1.20 respectively. Using this process, Quanbin *et al*., in 2006, extracted 33.2 mg chebulagic acid and 15.8 mg CA with a purity of 95.3 and 96.1% recovery from 300 mg of TC crude extract [3].

Mahajan *et al*., in 2010, isolated CA from TC by reverse phase high performance liquid chromatography (HPLC). They isolate 8 compounds gallic acid, methyl gallate, ethyl gallate, chebulagic acid, tetra-*O*-galloyl-*β*-D-glucose, ellagic acid, CA, and penta-*O*galloyl-*β*-D-glucose from TC. The purities were checked by spectroscopic methods. UV absorption maxima of the hydrolysable tannins obtained from TC is shown in Table 2 [4].

Pfundstein *et al*., in 2010, determined polyphenolic and other active constituents of TC and *Terminalia harridan*. It was reported that TC contained 61.8 g/kg of chebulic ellagitannins. Out of this chebulagic acid was 24.2 g/kg. Methyl neochebulinate, chebulic acid, chebulanin and methyl neochebulagate were present in decreasing order, in the range 7.1-9.0 g/kg. The recovery of CA was 4 g/kg along with small amounts of the partial hydrolyzed product (0.11 g/kg). Methyl neochebulanin is 2.2 g/kg. 32.2 g/kg gallic acid and gallate ester were present. The non-chebulic ellagitannins (25.0 g/kg) were represented by about equal amounts of corilagin and punicalagin. Ellagic acid was present at 4.1 g/kg [5]. In TC and its related plants, tannins are the main biologically active substances. They are present in different molecular forms such as dimers, tetramers and polymers, depending on the mode of extraction. In aqueous or ethanolic extracts the lower molecules are prevalent.

Klika *et al*., in 2004 extracted and isolate 1,3,6-Tri-*O*-galloyl-2,4-chebuloyl-*β*-D-glucopyranoside (CA) and its novel thrice hydrolyzed derivative, 2,4-chebuloyl-β-D-glucopyranoside (galloyl-free CA), together with ellagic and gallic acids, ethyl gallate, and luteolin, from the dried fruit of TC. They also identified and confirmed structure by UV, MS, and NMR data [14].

Table 1: Evidences of different varieties of TC in ancient Ayurvedic literature [11-13]

Serial number	Varieties of *Haritaki*	*Harita Shmita, Saligram Nighantu, Raj Nighantu, Bhav Praksh Nighantu*	*Raja Balabh Nighantu*	*Atreya Shamita*
1	*Abhaya*	Yes	Yes	Yes
2	*Amrita*	Yes	Yes	No
3	*Chetaki*	No	No	Yes
4	*Haimvati*	No	No	No
5	*Jaya*	No	No	No
6	*Jivanti*	Yes	Yes	Yes
7	*Kalika*	No	Yes	No
8	*Pathya*	No	No	No
9	*Putana*	Yes	Yes	Yes
10	*Rohani*	Yes	Yes	No
1	*Vijaya*	Yes	Yes	No

TC: *Terminalia chebula*

Table 2: UV wavelength of hydrolysable tannins [4]

Hydrolysable tannins	Physical property	UV λ max (nm)
Gallic acid	White amorphous powder	215, 271
Methyl gallate	White amorphous powder	215, 271
Ethyl gallate	White amorphous powder	215, 271
Chebulagic acid	Pale yellow powder	222, 276
Tetra-*O*-galloyl-*β*-D-glucose	Pale yellow powder	217, 278
Ellagic acid	White powder	253, 364
Chebulinic acid	Pale yellow powder	222, 276
Penta-*O*-galloyl-*β*-D-glucose)	Pale yellow powder	217, 278

UV: Ultraviolet

Mahajan *et al*., in 2011 found significant variation in active constituent of three market samples of TC churna. They used HPLC method for quantification and qualification of the sample. Due to this variation, it is better to use active constituent [15].

Hydrolysable tannins on treatment with hydrochloric acid and sulfuric acid yield gallic or ellagic acid [16].

***RASA PANCHAK*: PROPERTIES OF TC AS PER AYURVEDA**

Rasa (Taste) – Madhura, *Amla, Tikta, Katu*, *Kahasaya*
Guna (Property) – *Laghu, Ruksha*
Veerya (Dynamic property or Potency) – *Ushna*
Vipaka (Digestive stage) – *Madhur*
Prabhav (Distinctive action) – *Tridosha shamak*

The above mentioned different Rasas (taste) present in different parts of TC fruit.

Fruits of TC contain five *Rasas* (Taste),

1. *Madhur* – (sweet) - the fruit pulp
2. *Amla* - (sour) - the bulky portion of the fruit
3. *Tikta* – (bitter) - seeds
4. *Katu* – (Pungent) - the covering of the fruit
5. *Kahasaya* – (astringent) - the hard portion of the seed [7].

PHARMACOLOGICAL AND THERAPEUTIC ACTIVITIES

In ancient time, Charaka mentioned the use of TC in Javaraghna, Arsoghan, Kasaghan, Kusthaghna, Prajasthapana, while Susrutaused TC in Amalakyadi, Parusakdi, Triphala, and Vagbhatt used in Parusakadi. Gogotey has mentioned both internal and external uses. In external uses, it is mentioned that TC is used for inflammation, conjunctivitis and

it can used on the eyelids. Decoction of *Haritaki* is used for the washing of wounds. In combination with *Phyllanthus emblica* and *Terminalia bellirica* under the name Triphala, fruits of TC are extensively used as adjunct to other medicines in almost in almost all diseases [17]. Triphala had also been found to be anti-inflammatory activity in gouty arthritis [18].

Anti-inflammatory activity

Sabina *et al*., in 2008, in showed anti-inflammatory activity in monosodium urate crystal-induced inflammation in mice of Triphala. They showed its significance in gouty arthritis [18].

Reddy *et al.*, in 2009, showed that chebulagic acid is the compound in TC responsible for anti-inflammatory activity. They showed that chebulagic acid inhibit COX and 5-LOX responsible for anti-inflammatory and anticancer activity. Chebulagic acid showed potent COX-LOX dual inhibition activity with IC50 values of 15±0.288, 0.92±0.011 and 2.1±0.057 μM for COX1, COX2, and 5-LOX, respectively. They also showed apoptosis by chebulagic acid in COLO 205 cells. While ethanolic extract of TC showed IC 50 for COX1 and COX2 and LOX is 90 μg/ml, 3.75 μ, 20 μg/m [19].

Anti-viral activity

Extract of TC has antiviral properties [20]. Ma *et al*., in 2010, demonstrated the antiviral activity of acetone extract of TC. They used mixture of Tannic acid and TC, instead of a single compound in order to get synergistic action of mixture. They showed the activity of acetone extract against swine influenza A virus [21].

Anti-cancer activity

It is used traditionally as anticancer drug in Africa and Asia. Saleem *et al*., in 2002, showed *in vitro* anticancer activity of methanolic extract of TC. Cytotoxicity of *Terminalia* phenolics in HOS-1 cells was determined by the level of adenosine triphosphate (ATP). IC50 of CA was reported to be 53.2 μM [22]. Anticancer activity of 70% methanolic extract of TC was shown on cell lines of human (MCF-7), mouse (S115) breast cancer cell line, human osteosarcoma cell line, human prostate cancer cell line (PC-3), non-tumorigenic, and immortalized human prostate cell line (PNT1A). The parameters used to prove anticancer activity were proliferation thymidine incorporation and coulter counting. Cell viability was determined by ATP determination. The results revealed that concentration of 100 μg/ml, inhibit cell growth. It took some time to start its effect due to initiation of cellular processes causing decrease in proliferation and cell death. But at concentration of 400 μg/ml, it showed direct cytotoxic effect. The main components responsible for this action are CA, tannic acid, and ellagic acid [22].

CA is reported to inhibit HeLa cancer cell of cervical carcinoma. Although action of CA was restoration of gap junctional intracellular communication, exact mechanism is unknown [23].

Tannin extract of *TC* possess antimutagenic properties. Kaur *et al*., in 1998, showed that galic acid derivative and other tannins have antimutagenic activity against S9-dependent mutagen and 2AF in *Salmonella typhi* [24].

Prasad *et al*., in 2006, showed the chemomodulatory effect of TC in Wister rat against nickel induced oxidative stress. Nickel chloride treatment caused an increase in tumor promoters. The treatment of rat with TC with 25 mg/kg body weight dose reduces effect of nickel chloride. Thus, its extract can also be used in the prevention of cancer [25].

Chebulagic acid also has anticancer properties. TC is used to cure and stomach cancers [26]. It has 5-LOX inhibitory action 2.1±0.057 μM. It had demonstrated anticancer properties against HCT-15 (colon), COLO-205 (colon), MDA-MB-231 (breast), DU- 145 (prostate), and K562 (chronic myeloid leukemia) cancer cell lines. It also showed anti-proliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145, and K562 cell lines [19].

Cardiac effect

CA has anti-hypertensive properties. This effect may be due to decrease in cardiac output which causes reduced left ventricular contraction. Hydrolysable tannins potentiate activity of beta-adrenergic blocker by depressing muscle contraction [27,28]. Mitochondria play an important role at molecular level in ischemia. Pretreatment of alcoholic extract of TC at dose of 50 mg/100 g body weight had protective action in isoproterenol (ISO) (at dose 20 mg/100 g body weight) induced toxicity in rats. It was reported that TC retains normal function of mitochondria in ISO induced toxicity [29].

Antihyperlipidemic activity

TC has hypocholestemic effect. Thakur *et al*., in 1988 showed hypocholestemic effect in rabbits. Authors reported that TC has more lipid lowering activity than *Amla* and *Bahera* and it could be used as antihyperlipidemic agent for the treatment of atherosclerosis [30].

Antidiabetic activity

Aqueous extract of TC has been reported to have antidiabitic activity. Chebulic acid has protective action in case of glycation induced end product that causes endothelial cell dysfunction. According to Lee *et al*., in 2011, chebulic acid had IC50 values of 17.1 mM for protein cross-linking and 1.32 mM for advanced glycation end products (AGE) formation. As a positive control, aminoguanidine had IC50 values of 21.3 mM and 2.37 mM, respectively. They treat human umbilical vein endothelial cell with chebulic acid in the presence of AGEs. Due to chebulic acid dose-dependent reduction glycer-AGE induced formation to 108.2±1.9% for 25 μM versus 137.8±1.1% for glycer-AGEs treated alone. They showed chebulic acid may be an agent can be used in diabetic vascular complication [31].

Aqueous methanolic extract of TC has been reported to have alpha-glucosidase inhibitory action. This extract has been reported to inhibit the inhibitory action of maltase that is present in rat's intestine. Chebulanin, chebulagic acid, and CA have malatase inhibitory action with IC50 of 690, 97 and 36 μM, respectively. CA also has potent alpha-glucosidase inhibitory action. Thus, chebula and CA can be used in treatment and control of diabetes specially in type 2 diabetes [32].

It is also reported that TC possesses dose-dependent anti-diabetic activity in lowering blood glucose of streptozotocin induced diabetic rats [33].

Radioprotective action

TC extract has been found to possess radioprotective action in mice. Damage to DNA due to radiation was reduced [33,34]. TC along with other herbs (Triphala) is shown to be radioprotective properties at a dose of 10 mg/kg when administered intraperitonealy in mice. It acts by scavenging free radicals that are produced by radiation [35].

Anti-ulcer activity

TC has antiulcer properties. Sharma *et al*., in 2011, showed antiulcer activity [26]. It acts by inhibiting action of *Helicobacter pylori* by inhibiting urease activity which is responsible for ulcers in stomach. It

Table 3: Vehicles used for TC according to season [6]

Serial number	Seasons *(Ritu)*	Vehicle used for administration of TC *(Anupaan)*
1	*Illavenil* (midly sunny)	Honey
2	*Muthuvenil* (intense sunny)	Jaggery
3	*Kar* (cloudy rainy)	Rock salt
4	*Kuthir* (Cold)	Sugar
5	*Munpani* (Early misty)	Dried ginger
6	*Pinpani* (Late misty)	Long pepper

TC: *Terminalia chebula*

Table 4: Various patents on TC [43-88]

Serial number	Year	Publication number	Single/ Combination	Activity	References
1	Use of TC extract for treatment of osteoarthritis	US 20150174184	Single	Osteoarthritis	[43]
2	Plants parts and extracts having anticoccidal activity	EP 2866794	Combination	Control coccidiosis in poultry	[44]
3	TC and *Terminalia bellerica* extracts for inhibition of xanthine oxidase	US 20150050369	Combination	Uricemia, hyperuricemia, and gout in a human	[45]
4	Weight-reducing tea and preparation method thereof	CN 103976056	Single	Weight-reducing	[46]
5	Traditional Chinese medicine preparation for effectively treating dry cough	CN 103933435	Combination	Dry cough	[47]
6	Tea with function of smoking cessation	CN 103892005	Combination	Clearing throat and smoking cessation	[48]
7	Traditional Chinese medicine preparation for effectively treating dry cough	CN103933435	Combination	Dry cough	[47]
8	Broad-spectrum anti-toxic and bacteriostatic traditional Chinese medicine preparation and preparation method thereof	CN 103877320	Combination	Broad anti-virus range, strong bacteriostatic	[49]
9	Concentrated solution capable of clearing heat and removing toxicity	CN 103860859	Combination	Treating sore tongue and mouth, and swelling and pains in throat caused by internal heat	[50]
10	Plant parts and extracts having anticoccidial activity	CN20140161919	Combination	Coccidiosis in poultry and, more specifically, coccidiosis	[51]
11	Blood purifying mixture for treating skin diseases	CN103830379	Combination	Skin diseases	[52]
12	Physalisalkekengi heat-clearing throat-wetting wine and production method thereof	CN103815400	Combination	Hot cough, sound dumbness and other main syndromes	[53]
13	Compound tincture for treatment of porcine virus diarrhea, preparation method and application thereof	CN103800804	Combination	Treatment of porcine virus diarrhea	[54]
14	Blueberry wine with functions of invigorating stomach and relieving diarrhea and production method thereof	CN 103805422	Combination	Vomiting, nausea, abdominal pain and diarrhea	[55]
15	Traditional Chinese medicine effective part composition for treating chronic pharyngitis	CN103768138	Combination	Chronic pharyngitis	[56]
16	Traditional Chinese medicinal decoction for treating bronchial asthma	CN103751674	Combination	Bronchial asthma	[57]
17	Drug for treatment of rheumatoid arthritis and preparation method thereof	CN103751305	Combination	Rheumatoid arthritis	[58]
18	Traditional Chinese medicine preparation for treating tonsillitis and pharyngolaryngitis and preparation method thereof	CN103690695	Combination	Chronic pharyngolaryngitis and acute and chronic tonsillitis	[59]
19	Chinese herbal medicine feed for wide geese, wide ducks, African geese and wide chickens	CN103621837	Combination	To reduce diseases of the wide geese, the wide ducks, the African geese and the wide chickens and eliminate sanguinary smell and smell of meton and improve the immunity	[60]
20	Chinese medicine (TCM) for treating allergic rhinitis	CN 103610788	Combination	From relieving *Vibrio vulnificus* septicemia	[61]
21	Throat clearing and moistening healthcare tea	CN103493921	Combination	Allergic rhinitis	[62]
22	Plant parts and extracts having anticoccidial activity	WO/2014/004761	Combination	Anticoccidial activity	[63]
23	External powder for treating dental ulcer and preparation method thereof	CN103405578	Combination	Dental ulcer	[64]
24	TC compositions and method of extracting same	WO/2013/155175	TC	Antioxidant	[65]

(Contd...)

Table 4: ***(Continued)***

Serial number	Year	Publication number	Single/ Combination	Activity	References
25	Inhibitor and a breaker of an AGE-products - induced crosslink, containing chebulic acid as an active ingredient	Kr 1020130109874	TC	Antioxidant	[66]
26	Mouthwash composition for managing oral mucositis, process and methods thereof	US20130243702	Combination	Oral mucositis	[67]
27	Quality control method of drug for treating cough	CN103175938	Combination	Treating cough	[68]
28	Cosmetic composition containing Indian natural products for skin whitening	Kr 1020130057542	Combination	Skin whitening	[69]
29	A Chinese medicinal formulation for treating infiltrative pulmonary tuberculosis	CN102847026	Combination	Pulmonary tuberculosis	[70]
30	A Chinese medicinal formulation for treating tuberculosis of intestine	CN102847027	Combination	Tuberculosis of intestine	[71]
31	Traditional Chinese medicine for treating fungal skin infection	CN102824518	Combination	Skin fungal infection	[72]
32	Traditional Tibetan medicine for treating alopecia	CN102784216	Combination	Alopecia	[73]
33	Traditional Chinese medicine preparation for treating viral enteritis and diarrhea	CN102670936	Combination	Viral enteritis and diarrhea	[74]
34	Herb extract for cognitive health benefit	EP2486932	Combination	Cognitive health benefit	[75]
35	Antioxidant active compound of TC and preparation method thereof	CN102526136	Single	Antioxidant activity, tyrosinase inhibitory activity, bacteriostatic action and cell protection effect	[76]
36	Hair treatment composition	EP2467191	Single	Permanent hair dye	[77]
37	Hair treatment composition	US20120138079	Single	Hair dye	[78]
38	A mouthwash composition for managing oral mucositis, process and methods thereof	WO/2012/059874	Combination	Oral mucositis in cancer patients	[79]
39	Plant extracts, compositions containing same, and uses thereof	US20120027697	Combination	Cosmetics	[80]
40	Chinese composition for treating rhinitis	CN102284035	Combination	Rhinitis	[81]
41	Pharmaceutical composition containing TC retzius extract for or treating dermatitis	Kr1020110108825	Single	Dermatitis	[82]
42	Screening method (metabolite grid) for therapeutic extracts and molecules for diabetes	US20110159118	Combination	Diabetes	[83]
43	NF-kappa B inhibitor containing TC fruit extract	Kr1020110073241	Single	NF-kappa B activation increase-associated diseases	[84]
44	Compound TC Retz. throat lozenge and preparation method thereof	CN102100326	Single	Reducing fever, relieving the sore throat and promoting the production of the body fluid and has the advantages of excellent mouth feel	[85]
45	Method for preparing TC extract for preventing or treating prostate cancer	Kr1020110048133	Single	Prostate cancer	[86]
46	Hair treatment composition	WO/2011/020833	Single	Permanent hair dye	[87]

TC: *Terminalia chebula*

is reported that aqueous extract has strong anti *H. pylori* activity.It also improvers the activity of bruneres gland, thus helpful in the treatment of duodenal ulcers [33].

Anti HIV activity

CA present in TC has anti HIV properties. CA act by inhibiting binding of HIV rgp20 to CD4. CA was found to non-toxic at dose up to 10 times [36]. Several hydrolysable tannins inhibit the expression of HIV antigen present in human lymphotropic virus type 1-postive MT-4 cells. These tannins inhibit HIV adsorption on cells [37].

Antioxident activity

Aqueous extract of TC has antioxidant properties. Extract of *TC* is found to have more antioxidant properties than *Momordica charantia, Glycyrrhiza glabra,* and *Acacia catechu.* Aqueous extract of TC had antioxident activity by IC50 by thiobarbituric acid reactive substances is 14.5 µg/ml, IC50 by DPPH is 11.5 µg/ml, and ascorbate equivalent is 60% [38].

Chebulagic acid has antioxidant properties. It has DPPH radical scavenging activity with IC50 of 1.4 µM and strong inhibition of ABTS radical with an IC50 value of 1.7±0.023 µM [19].

TC had antioxidant properties due to the presence of hydrolysable tannins [39]. Tannins were found to have more potent antioxidant activity than flavonoids [40]. Chebulinic and chebulagic acid, both were found to have antioxidant properties [14,19,41]. CA has been reported for better antioxidant activity than other tannins due to higher DPPH activity [5].

Hepatoprotective action

TC extract has hepatoprotective action against rifampicin, isoniazid, and pyrazinamide toxicity [33]. Hydrolyzable tannins generally exhibit an intense enzyme inhibitory action on glutamic-pyruvic transaminase [42].

Miscellaneous

Adrenocorticotropic hormone-induced lipolysis could be enhanced by CA and tellimagrandin I at 5-100 g/ml [41]. TC and its extract are used in wound healing and as antispasmodic. It has antibacterial properties also. It is used as anticaries agentin mouth washes. It has been used to treat respiratory disorders in Ayurveda. It is also reported to be used in urticarea and skin allergies. It has also been found to have purgative and antiamoebic action [26,33].

FORMULATIONS AND PREPARATIONS

TC is a rejuvenating medicinal fruit and it is used with different vehicles for the rejuvenation of body. Different formulations and ayurvedic preparations of TC available are *Abhayamodaka, Abhayarishta, Pathyadivati, Pathyadikwath, Vyaghriharitaki, Haritikileha, Chitrakharitaki, Agastiharitaki, Dantiharitki, Haritakikhanda, Pathyadichurna, Abhayadiguggulu, Abhayadikalka, Amritaharitaki, Abhyaamalakiyarasayana,* and *Kayakalpa*. To act as *Kayakalpa,* it should be consumed with different vehicles according to the season as shown (Table 3) [6]. Various patents related to TC are depicted in Table 4.

From the medicinal point of view, most of tannins of TC bring good results. They are effective against bacteria, viruses, parasites, and cancer cells. They protect animals and organs with their antioxidant property. They are reported to be nearly not toxic. But because there are no dosages known for the use in humans, they cannot be recommended for the internal use in humans [26]. YI *et al*., in 2004, showed that IC50 of CA for erythroid differentiation was 40 µmol/L for hemin-induced cell and 4 µmol/L for BA induced cells, respectively. CA has an inhibitory effect on erythroid differentiation of K-56 cells [88].

CONCLUSION

TC is a unique herb having various therapeutic potential as anti-inflammatory, antioxidant, anticancer, and digestant. Classification, chemical constituents, therapeutic uses, and patents that have been reported for TC. Various pharmacological activities of TC that make it as potential medicine and its Ayurvedic formulations are highlighted.

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