

Bitter apple (*Citrullus colocynthis*) - A review of a wild plant growing from Asia to Africa with high medicinal potentials

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Abstract

Bitter apple (*Citrullus colocynthis*) is a perennial herb belonging to kingdom "plantae", division "Magnoliophyta", class "Magnoliopsida", order "Cucurbitales", family "Cucurbitaceae" and genus "Citrullus". It is a drought resistance plant that possesses enough potential to bear severe water shortage and known with different names in different regions of the world. *Citrullus colocynthis* is a desert plant that requires arid and sandy soils and is found native to Asia and Mediterranean Basin and also distributed in west coast of North Africa. Seeds of *Citrullus colocynthis* are a rich source of fatty acids such as palmitic acid, stearic acid, oleic acid, linolenic acid and linoleic acid. Some major chemical constituents of *Citrullus colocynthis* are docosan-1-ol acetate, 0,13-dimethyl-pentadec-13-en-1-ol, 11,14-dimethyl hexadecane, 14-ol 2-one, 10,14-dimethyl hexadecane 14-ol 2-one, linoleic acid, oleic acid, carbohydrate, amino acid, organic acid, lipid, sterols and phenols. Numerous bioactive compounds are also present in the *Citrullus colocynthis* which are grouped as essential oils along with glycosides, flavonoids, alkaloids, fatty acids and carbohydrates. Due to the presence of various bioactive components, extracts and essential oils of this plant are used to cure ascites, ulcers, tumours, leucoderma, bronchitis, jaundice, asthma, urinary discharges, enlargement of the spleen, tuberculosis glands of neck, dyspepsia, constipation, anaemia, throat diseases and joint's pain elephantiasis.

Key words: *Citrullus colocynthis*, perennial plant, desert plant, bioactive compounds, alkaloids, flavanoids, glycosides, fatty acids

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1. Botany

1.1 Introduction

Bitter apple (*Citrullus colocynthis*) is perennial herb belonging to kingdom plantae, division Magnoliophyta, class Magnoliopsida and order Cucurbitales, family Cucurbitaceae and genus Citrullus [1]. The first scientific name of bitter apple was *Colocynthis citrullus* but later it was changed by *Citrullus colocynthis*. This plant family is tolerant to draught and intolerant to poorly drained and wet soils and also sensitive to frost [2]. Among the well-known members of the Cucurbitaceae family are gourd, cucumber, pumpkin, melon and bitter apple. The pollination in *Citrullus colocynthis* usually takes place by insects and the fruits of this plant are the indehiscent smooth barriers which are ready for harvesting just after three to four months of planting. *Citrullus colocynthis* has different common names in different countries e.g "Hanjal" in Urdu, "Bitter Apple" in English, "Indrayan" in Hindi, "Anedri" in Sanskrit, "Kattu Kattu Vellari" in Malayalam, "Pcittumatti" in Tamil and "Rakha" in Bengal [3]. This plant is traditionally used for medicines, for the treatment of asthma, jaundice and diabetes. With the passage of time, the consumer awareness

Jabeen et al., 2017

and production of cucurbit plants is being increased due to health benefits [4]. *Citrullus colocynthis* is a valued cucurbit plant which is mainly distributed in deserted areas of world, especially Pakistan having nutraceutical and medicinal values [5]. From last two to three decades, China and India have been the largest producers of cucurbit plants followed by USA, Egypt, Iran and Russia [6].

1.2 History/Origin

Citrullus colocynthis belongs to deserts. It is a viny plant which grows in the sandy and arid soils. *Citrullus colocynthis* is native to Asia and Mediterranean Basin and also distributed in west coast of the North Africa [7]. It is also distributed in Egypt, Sahara and India. It is also spread in north coast of Caspian, Mediterranean Sea and islands of Grecian archipelago. It is also cultivated on small scale in island of Cyprus [2].

1.3 Location

Citrullus colocynthis Schard belongs to the family Cucurbitaceae and native of Asia and Africa found in Syria and Egypt. It was cultivated in Spain and occurs throughout the India, particularly in Tamil Nadu, Gujarat and Punjab. It was an annual plant resembling the common watermelon.

Bhakkar is located in the south of Punjab Province (Pakistan) including three subdivisions (Bhakkar, Kallurkot and Mankera). It is located between 31°09' to 32°12' North latitude and 70°19' to 71°58' East latitudes with a total area of 3,134 square miles. The district has extreme climate with sizzling hot summer. The maximum temperature goes upto 42°C with a minimum to 28°C. The hottest months are June, July and August. Winter is equally cold and frosty with maximum at 10°C and minimum below freezing point [8].

1.4 Morphology

Citrullus colocynthis shows alternately angular leaves present on long petioles. Leaves are 5 to 10 cm long and lobes can be 3 to 7 having middle lobe with ovate structure. The leaves also have triangular shape and number of clefts. The texture of leaves is rough and hairy having open sinuses. Leaves show two colours in surfaces, upper surface is green and lower is pale yellow. Leaves show variability in their sizes. The cultivated leaves are larger in size but the wild leaves are smaller in size ranging from 3.8 to 6.3 cm in length and 2.5 cm in width. *Citrullus colocynthis* produces 15 to 30 fruits globular in shape having diameter ranging from 7 to 10 cm. Fruit is enclosed in green skin, showing yellow strips and inner fruit also shows yellow color. When this fruit is ripened, it shows hard and thin rind [9]. Pulp of the fruit is bitter, white, spongy and soft having compressed ovate seeds. At the axils of leaves, single yellow flowers are present. Flowers are monoecious, having pistils and stamens in the same plant. Flowers are attached with long peduncles, having five lobes of corolla and five ways of calyx. The female flowers can easily be distinguished from male flowers. The ovary present in female flowers is villous and hairy. *Citrullus colocynthis* seeds are smooth, ovoid-shaped, compressed and 6 mm in size. Seed colour varies from dark brown to orange yellow attached on parietal placenta. *Citrullus colocynthis* roots are perennial, tough vine like, slender, angular and long. The stems of this plant spread on ground showing ability of climbing on the other herbs and shrubs because of their axillary branching tendrils [10].

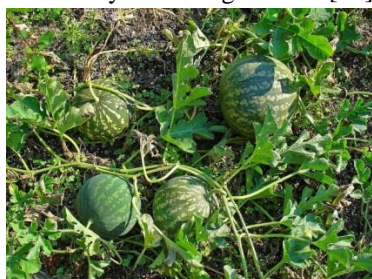


Fig 1 Bitter Apple (*Citrullus colocynthis*) grows in wild

2. Chemistry

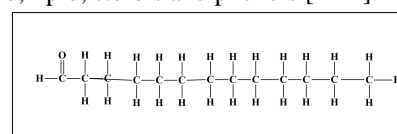
The seeds of *Citrullus colocynthis* are rich in fatty acids like palmitic acid, oleic acid, stearic acid, linoleic acid and linolenic acid. It has been reported that de-oiled cake of *Citrullus colocynthis* is incorporated in cattle feed ranging from 20% to 25%. So there is not any significant change in the yield of the milking cows. The composition of tumba

Jabeen et al., 2017

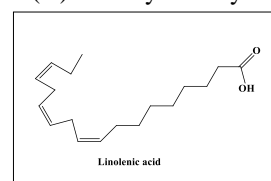
seed oil is similar to soybean oil, so it is also edible like soybean oil. To remove its bitter taste, it is washed with citric acid. Seeds germinate in dark at 30°C, so the amount of fatty acids is increased significantly during the germination but the amount of triacyl glycerol is decreased. Hence, it was also observed that the amount of saturated fatty acids is increased gradually during the germination while the amount of unsaturated fatty acids is decreased [11].

2.1 Chemical Composition

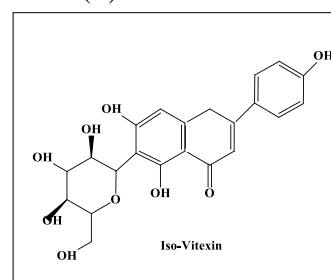
The main chemical constituents of *Citrullus colocynthis* reported in the literature are docosan-1-ol acetate, 0,13-dimethyl-pentadec-13-en-1-ol, 11,14-dimethyl hexadecane, 14-ol 2-one, 10,14-dimethyl hexadecane, 14-ol 2-one, linoleic acid, oleic acid, carbohydrate, amino acid, organic acid, lipid, sterols and phenols [1-11].



(A) Tridecyl aldehyde



(B) Linolenic acid



(C) Iso-Vitexin

Fig 2 Chemical structures of some potential phytochemicals (A) Tridecyl aldehyde (B) Linolenic acid and (C) Iso-Vitexin

2.2 Phytochemistry

A number of bioactive compounds are present in *Citrullus colocynthis* which are grouped as essential oils, glycosides, alkaloids, flavonoids, fatty acids and carbohydrates. But only few reports are present on isolation of individual chemical constituents and their identification. The main components of *Citrullus colocynthis* are Cucurbitacins. Cucurbitacins are bitter in taste, tetracyclic, oxygenated, triterpenic substances which are derived from skeleton of cucurbitane. Cucurbitacins are usually predominantly present in family of Cucurbitaceae. Cucurbitacins contain total twelve categories but all these categories are not present in *Citrullus colocynthis*. Because of their cytotoxic behaviour, they play important role in discovery of drugs especially for the anticancer drug

development. It is mainly present in the pulp of this fruit [12].

Table 1 Amino acid composition of *Citrullus colocynthis* seed flour [1]

Amino Acid	Conc. (g/100g of protein)
Lysine	0.4g
Glycine	2.2g
Arginine	9.0g
Serine	2.4g
Threonine	3.1g
Histidine	2.0g
Cystine	1.1g
Glutamic acid	16.9g
Alanine	5.6g
Proline	3.2g
Methionine	0.3g
Isoleucine	4.8g
Phenylalanine	3.2g
Aspartic acid	16.3g
Tyrosine	2.2g
Leucine	4.2g
Valine	1.3g

Table 2 Mineral composition of *Citrullus colocynthis* seed flour [1]

Mineral	Concentration (g/100g)
Sodium (Na)	13.0 g
Potassium (K)	96.1 g
Calcium (Ca)	28.2 g
Magnesium (Mg)	31.4 g
Manganese (Mn)	1.7 g
Copper (Cu)	0.4 g
Zinc (Zn)	1.2 g
Iron (Fe)	1.3 g
Phosphorous (P)	125.3 g

3. Postharvest Technology

All year round, seeds of this plant are available. This is because it is dried after harvest; in this state, it can be stored for a very long time. Cultivation is at the beginning of the rainy season, in the months of April through June, either on ridges or on flat ground in holes about 75-90 cm apart. It is harvested at the onset of the dry season, in the months of October through December. In Nigeria, this crop is grown mainly in three ecological zones: these are the forest zone, the derived savanna zone (reclaimed from forest) and the southern Guinea savanna zone, where it is usually grown in conjunction with tuber and cereal crops. Two or three seeds are usually sown per hole and seedlings appear 4-7 days after sowing. As a result of the plants' spreading habit, early ground cover is attained which enhances weed suppression [13].

4. Pharmacological Uses and Therapeutic Potentials

4.1 Medicinal Values

Fruits are pungent, bitter and purgative in nature thus acts as antipyretic, anthelmintic and carminative and *Jabeen et al., 2017*

used to cures ascites, tumors, ulcers, leucoderma, bronchitis, asthma, jaundice, urinary discharges, tuberculosis glands of neck, enlargement of spleen, constipation, dyspepsia, throat diseases, anemia and joint's pain elephantiasis. Roots of *Citrullus colocynthis* are useful in remediation of ascites, jaundice, urinary diseases and given in abdominal enlargements and in cough and asthmatic attacks of children. Root is also useful in the inflammation of breast. Root or fruit is rubbed to form a paste with water and applied to pimples and boils. *Citrullus colocynthis* is also very important for traditional use in the remedy for carcinoma, cancer, leukemia, endothelioma and tumors of eye, spleen and liver [14]. Decoction of whole plant prepared with juice of the fennel is helpful for indurations of liver. The roots are also used as purgative against urinary diseases, jaundice, snake poison and rheumatism. The plant is found in southern coastal area of Bay of Bengal. Traditional methods of screening are most commonly used for the study of pharmacological effect of their phytochemical constituents. *Citrullus colocynthis* is commonly termed as bitter apple, colocynth and bitter cucumber. This is desert, viny plant which is native to Asia and Mediterranean basin [15]. It shows resemblance with watermelon vine but has hard and small fruit with bitter pulp. *Citrullus colocynthis* has also been used in folk medicines for centuries and also as the source of energy e.g. biofuel and oil seed.

4.2 Pharmacological Uses

Same quantities of the fresh *Citrullus Colocynthus* roots and *Piper nigrum* L. are ground with small amount of water to make fine paste of both. One gram of paste is used three times daily for atleast three days for the treatment of abdominal pain. Fresh *Citrullus Colocynthus* roots are boiled in the cow's milk in a ratio of 1:8.5 ml of milk is orally administered two times daily for forty-one days for the treatment of amenorrhoea [12]. Raw fruits and fresh roots of *Citrullus Colocynthus* are used to make a fine paste. This fine paste is applied thoroughly, externally two times daily for the treatment of carbuncles and boils. Paste of fresh *Citrullus Colocynthus* roots, by grinding the fresh roots with little water is applied to the chronic wounds three times daily till it is healed completely [16]. Decoction of the fresh fruits of *Citrullus Colocynthus* is prepared using water in the ratio of 1:6.5 ml decoction is then administered orally, at bed times for atleast three days for the treatment of constipation. Pericarp or ripened fruits of *Citrullus Colocynthus* are boiled in the Sarson or Mustard Oil with scientific name (*Brassica campestris* L.), Family (Brassicaceae) in the ratio of 1:7.3-4 drops of this prepared oil are applied in affected ear two times daily for the treatment of deafness till the ailment is completely cured.

A decoction is obtained after boiling the chopped ripened fruits of *Citrullus Colocynthus* in the water in ratio of 1:6. It is then used for mouth wash two times daily for at least seven days for the treatment of dental caries [12].

Ajawain with scientific name *Trachyspermum ammi* (L.), Spr. Family-Apiaceae and sodium chloride (NaCl) are equally mixed and stuffed in the ripened fruits of *Citrullus Colocynthus* via a hole in the pericarp. Both fruits are dried until crispness in the sun and the ground to form a fine powder. From quarter to the half gram of powder is used after each meal atleast for the forty days for the treatment of dyspepsia. Fresh *Citrullus Colocynthus* roots are boiled using water in the ratio of 1:5.5 ml of decoction is used two times a day for atleast seven days for the treatment of painful micturition. Fresh fine roots paste of *Citrullus Colocynthus* can be applied externally on the lower abdomen, two or three times daily for the treatment of dysuria [17]. Treatment must be continued till the complete cure is acquired. Ripened *Citrullus Colocynthus* fruits, stuffed with the *Piper nigrum* L., (Family-Piperaceae) via a hole in the pericarp. Each of fruit is finely covered with the mud and also baked in the cow-dung fire and wait till its colour becomes red.

Ash of *Citrullus Colocynthus* fruit and the black-pepper are both collected and also stored. Half gram ash is used after each meal daily for fifteen days for the treatment of flatulence. Part fresh root of *Citrullus Colocynthus* is boiled in six parts of "Arandi ka tel" (seed oil, *Ricinus communis* L., Family-Euphorbiaceae). Two ml oil so obtained is mixed with 250 ml cow's milk and given twice a day for 15 days for the treatment of hydrocele. Chopped fresh roots of *Citrullus Colocynthus* with pulp of the ripened fruit (*Aegle marmelos* (L) Corr., having Family-Rutaceae), both are mixed in equal amounts and are boiled in the cow's milk in ratio of 1:6.2 ml milk is used two times daily for atleast three months or till the time menses become regular for the treatment of infertility [17]. Fine fresh roots paste of *Citrullus Colocynthus* obtained by the grinding roots with little water is applied two times daily on the sore nipples or inflamed mammary glands for the treatment of inflamed mammary glands till completely cure is obtained. Leaf extract obtained by squeezing the pounded leave in muslin cloth is applied to the affected area of skin for the treatment of leucoderma, for two or three times daily.

Seed oil can be applied to the depigmented areas for every 3rd day. Therapy is continued till pigments are reappeared and becomes stable. This is reputed therapy for the leucoderma in study area. Fresh roots paste of the *Citrullus Colocynthus* is applied externally two times daily. Therapy continues for 8 days in the acute cases and in the chronic cases it has recommended till the completely cured is achieved for the treatment of paronychia [18]. Matured *Citrullus Colocynthus* seeds have to be compressed for extracting oil. Regular applications of the oil is also claimed to impart the natural black color to grey hair for the treatment of premature greying of hairs. Fresh roots of *Citrullus Colocynthus* and *Withania somnifera* (L.), diurnal plant of family Solanaceae, both are taken in the equal quantities and are grind to form a fine paste. Approximately,

2g paste is mixed with the 5g honey is used orally two times daily for the treatment of rheumatism till completely cure is achieved. Therapy is very effective and it is also claimed that the patients begin to improve in only two days of the therapy. Roots of *Citrullus Colocynthus* are grinded to form a fine paste. Almost 2 g paste is applied to a pan leaf *Piper betle* L., Family Piperaceae and then it is used orally within only 2 hours of the snake bite [18].

Around 150 g of the chopped plant is boiled in 2 liters water until volume is reduced to the one fourth. Half litre seed oil of *Ricinus communis* L., family Euphorbiaceae is added to this decoction and boiled again to evaporate the water completely. Oil is stored in the black glass bottle. About 2 ml oil is mixed with the 250 ml cow milk and is given to the patient orally two times daily for the treatment of syphilis till completely cure is achieved. Fresh roots paste of *Citrullus Colocynthus* can be applied to the genitalia to induce the labour. Decoction of the fresh fruits of *Citrullus Colocynthus* is prepared in water using 1:6, ratio. Similarly, 2 ml decoction can be administered orally two times a day for complete 7 days to promote lactation. This plant is abortifacient in nature as fresh root of *Citrullus Colocynthus* must be ground to form a fine paste and then applied over vagina [18]. Almost 2g paste must be given orally one time daily for the termination of pregnancy. Fresh *Citrullus Colocynthus* root is boiled in cow's milk in ratio of 1:6. Approximately 2ml is used orally two times daily for the treatment of vaginal pain. Fresh *Citrullus Colocynthus* roots are grind to form a thin paste and then applied to affected part. Fruits and roots with nux-vomica are rubbed to form a paste mixing with water. Paste is applied on pimples externally, till completely cure is achieved.

Roots of "Tumba" are ground to form a paste and used for the treatment of enlarged abdomen of children. Decoction of plants is made in the juice of the fennel. Two ml juice is used orally two times daily for three days for the treatment of indurations of liver. Juice of the fruit must be mixed with the sugar. Then juice is used orally two times daily for three days for the treatment of dropsy. Mature *Citrullus Colocynthus* seeds can be compressed for the extraction of oil and used for the treatment of bowel complaints. Fresh pulp of the *Citrullus Colocynthus* seeds is eaten two times for two days for the treatment of malaria. Fresh roots of *Citrullus Colocynthus* with *Tylophora indica* and leaves of *Securinega leucopyrus* can be crushed together. One tea-spoon of the extract can be administered two times daily for five days for the treatment of cough. Fresh fruits of *Citrullus Colocynthus* are collected, stuffed with the salt and Ajawain. Fruits are then dried and grind to make the powder. Two grams powder is used orally two times daily for two days for the treatment of stomach ache [19].

Fruit pulp of *Citrullus Colocynthus* is mixed with Ajawain seeds and mixture is kept for 7 days and dried in the shade and ground to powder. Two gram powder is used

orally two times daily for three days for the treatment of jaundi. Pulp of ripened *Citrullus Colocynthus* fruit is trampled by the naked feet till the feelings of bitterly taste is appeared in mouth for fifteen days for the treatment of diabetes. Dry pulp of *Citrullus Colocynthus* fruit is kept in the water overnight in earthen pots. Then, this can be used for the regular washing of the anal parts for the treatment of piles after the nature's call in morning time. Seeds of *Citrullus Colocynthus* are useful in scarcity. Bittered seeds buried in the common salt (NaCl) to wash off bitter principles then dried and mixed with the bajra seeds and then mixed flour is used for the treatment of scarcity [19]. Leaf juice of *Citrullus Colocynthus* is applied on the body for the quick healing of wounds. Leaf juice of *Citrullus Colocynthus* is boiled with the pure mustard oil. It is filtered and then massaged on all the body before taking bath for the treatment of skin lice infection. Fruits of *Citrullus Colocynthus* are used orally for gastric problem. Shade dried roots of *Citrullus Colocynthus* are converted to a paste and this paste is given in the hemorrhoids [20].

Summary

The desert plant *Citrullus Colocynthus* is a perennial herb that grows well in sandy and arid soil conditions and mostly found in Northern areas of India, Egypt and Sahara. It is well-known medicinal herb of all traditional systems of medicines due to its excellent therapeutic potentials. It is known to possess strong anti-microbial, anti-diabetic, anti-inflammatory, anti-cancer and larvicidal activities along with strong local anesthetic potentials. Therefore this medicinal plant is extensively used to treat asthmatic attacks of children, cough, abdominal enlargements, urinary diseases, jaundice, ascites, joint's pain elephantiasis, anemia, throat diseases, dyspepsia, constipation, enlargement of spleen, tuberculosis glands of neck, urinary discharges, jaundice, asthma, bronchitis, leucoderma, ulcers, tumors, ascites and many other diseases. In short, it's a plant of great commercial importance so should be planted properly.

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