**AN OVERVIEW OF CITRULLUS COLOCYNTHIS**

**Dr.B.PRATHAP, DEVIKA.M, CHRISTINA SELVI.P, DHARANI.C, DINESH.K, DIVYA.R**

**Department of Pharmaceutical Analysis, Dhanalakshmi Srinivasan College of Pharmacy, Perambalur, Tamil Nadu. 621 212**

**ABSTRACT**

Citrullus colocynthis (L). schrad (C.Colocynthis), often known as *Colocynth.* [FAMILY : *Cucurbitaceae*]. It is commonly found wild in the sandy lands of North West, Punjab and central and Southern India and Coromandal cost. Fruit is Bitter, Pungent and the Fruit are used as a Purgative, anthelmintic, leucoderma, ulcers, asthma etc. Root is useful in Jaundice, ascites, urinary disease, rheumatism. The Pharmacological effects of Root, Fruits, Seeds, Leaves, and the whole *Citrullus* *Colocynthis* have been practiced for the treatment of disease. The aim of the study: The present research was undertaken to investigation the Pharmacological activities, Botanical description, Biological sources, Geographical sources, Taxonomic classification, characteristics, Morphological, Nutritional value, Ayurveda and Siddha action. Citrullus colocynthis fruits are containina glycosidees, flavanoids , fatty acids.

**Key words**

Citrullus Colocynthis, Colocynth, Cucurbitacins, Pharmacological activities, Bitter apple.

**INTRODUCTION**

Citrullus Colocynthis (Bitter apple) is a useful cucurbit plant that is extensively dispersed throughout the world’s arid location. [ family: Cucurbitaceae]. Commonly found wild in the sandy lands of the Punjab, southern India, North West, and Coromandel coast. This Plant is a mainly found in the desert of Arabia and the Sahara and the Southern part of Asia, which is mainly include India, Pakistan, Southern, Island. It originally bore the scientific name Colocynthis Citrullus. Citrullus Colocynthis shows the presence of Male and Female flowers. Mature fruits have tiny seeds and are about 6mm long, oval in shape, compact in structure, Brownish in Colour and Smooth in texture. Male flowers: Peduncles long villous, calyx tube broadly campanulate, pale yellow, segments obovate, apiculate. stamens 3 short, free anther, cohering, 1-celled, other 2-celled. Female flowers Calyx and corolla as in male 3 legulate stamens, ovoid ovary with 3-placentiferons and many compressed ovules are present. Plant products are often used in medicinal herbs sinces the very beginning, leaves of the plant, flowers, petals, root system, fruit extract, seed residue and seed pods can be used to prepare medicines and herbal products and it can also be used in the food industry. Leaves are variable, pale green above, ashy beneath, usually deltoid in outline, three lobed, lobed deeply pinnate. Leaves are variable in size. Fruits are globular in green in colour and get white glabrous when ripe. Fruits are filled with a dry spongy very bitter pulp. The fruits has been used to treat disease such as Diabetes. Seeds are pale brown colour. This plant is also used as a remedy for gastrointestinal disorders like indigestion, gastroenteritis and intestinal parasites. Different parts of these plants serve as a therapy for disease such as Jaundice, asthma, diabetes. This plant is also used to treat diabetes, liver problems and weak bowel movement.

**BOTANICAL DESCRIPTION**

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**Fig: 1**(citrullus colocynthis)

**Synonyms**

C.Colocynthis many common name including *Abu* *Jahl’s* *Melon*,

Colocynth, Bitter apple, Bitter cucumber, Egusi, vine of Sodom ( or ) wild gourd .

|  |
| --- |
| Colocynthis vulgaris schrad.  Cucumis colocynthis L.(basionym)  Citrullus pseudocolocynthis M. Roem.  Colocynthis officinalis schrad. |

**Biological sources**

Dried pithy pulp of the ripe fruits of *Citrullus* *colocynthis* *Schrade* [ FAMILY ; *Cucurbitaceae*]

**Common name of Citrullus colocynthis Root**

Citrullus colocynthis root English name is Bitter Apple Root, in Hindi, it is Indrayan Mool, it has many common names like Biteer Cucumber, wild gourd, Tumba ki jad.

It is a desert Viney plant that grows in sand, its fruits and roots are used in Ayurveda for medicinal purposes.

**Taxonomic classification**

Kingdom - Plantae

Sub kingdom - Tracheobionta

Super division - Spermatophyta

Division - Magnoliophyta

Class - Magnoliopsida

Sub class - Dilleniidea

Order - Cucurbitales

Family - Cucurbitaceae

Genus - Citrullus

Phylum - Embryophyta

Species - Colocynthis

**MORPHOLOGICAL CHARACTERISTIC**

|  |  |
| --- | --- |
| Roots and Stem | Perennial roots, stems are angular, tough and rough vine-like that spread on the ground and may climb up. |
| Seeds | Yellow to brown in colour, smooth in texture and oval in shape. |
| Flowers | A single yellow colour flower at leaf axils. They are monoecious and have long peduncles. |
| Fruit | Angular and about 5-10cm long. They are triangular, rough and green. |



**Fig: 2** (A) seeds (B) roots (C) plant (D) leaf (E) flower and (F) fruit of citrullus colocynthis

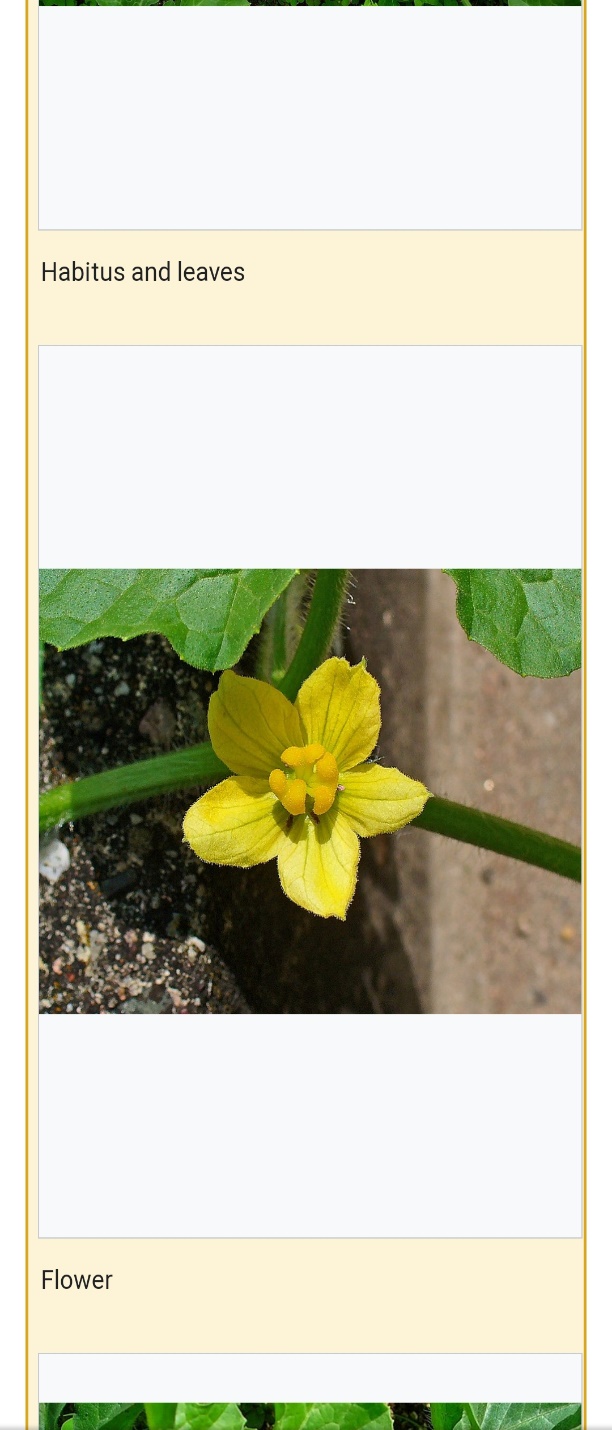
**Roots and Stem**

The roots are large and fleshy with long tap roots for high survival. The bitter apple plant has a large perennial root that sends out long and slender , scabrid, ( slightly rough to the touch) angular , tough , rough vine like stems .It is usually lying on the ground, The stems are normally spread on the ground, if shrubs or herbs are present use secondary branching vines to climb.

**Flowers**

The yellow-coloured flowers appear singly at leaf axils. The female flowers are easily identified from the males by their villous, hairy ovary . The calyx of male fl1owers is shorter than the corolla. There are 5 stamens, 4 of which are united and 1 is solitary, with a piece of anther. Males and Females can be distinguished by observing the spherical, hairy lower ovary of the female flowers.

Flowering period: May, June, July, August.



**Fig:3** (Flower of citrullus colocynthis)

**Fruits**

The fruits are smooth spheres 5-10 cm in diameter and have a very bitter taste. The calyx encloses the yellow-green fruit and becomes marbled with yellow stripes at maturity. Each bitter apple plant produces around 15 to 30 globular fruits having a diameter of almost 7 to 10 centimeters. The outer portion of the fruits is covered with a green skin having yellow stripes. The fruits may also be yellow in colour. Each of the 3 carpels contains 6 seeds. Each plant produces 15-30 fruits. The mesocarp is filled with a soft, dry spongy, white pulp in which the seeds are embedded.



**Fig: 4** (fruit of citrullus colocynthis)

**Leaf**

The angular leaves are alternately located on long petioles. Each leaf is almost 5 to 10 cm in length and has around 3 to 7 lobes. Sometimes the middle lobe might have an ovate structure. The leaves have a triangular shape with many defects. The leaves have a rough, hairy texture with open sinuses. The upper surface of the leaves is fine green in colour and the lower surface is comparatively pale.

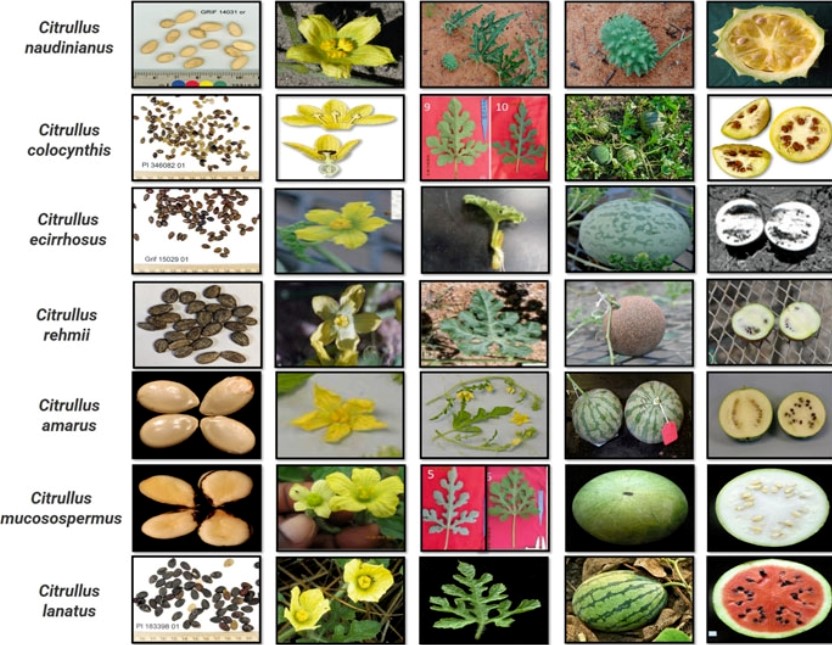
**Seeds**

It has an equally bitter nutty flavour and is rich in fat and protein. Seeds are grey, 5mm (1/4 inch) long and 3mm (1/8 inch) wide. They are located on the parietal placenta. The seeds are light yellowish orange to dark brown in colour.

**Similar Species**

It resembles a watermelon of the same genus.

**VARIOUS SPECIES OF CITRULLUS**



**Fig: 5** (varies species in citrullus genus)

**CULTIVATION**

A perennial plant, citrullus colocynthis can be propagated by both reproduction and vegetative means. However, seed germination is poor due to extreme dry conditions, and vegetative propagation is more common and successful in nature. In the arid regions of India, growth occurs between January and October, but the best time for vegetative growth is summer, which coincides slows as soon as it rains and cools, and almost causes during the cold, dry months of December and January. Growth prefers sandy soil and is a good example of good water management, and may also be useful for research to better understand how desert plants respond to water stress. Organic fertilizers can be applied to increase production colocynth is commonly grown (intercropped) with cassava in Nigeria. Cultivated colocynths like other crops suffer from climate stress and diseases such as cucumber mosaic virus, melon mosaic virus and fusarium wilt. To ameliorate that, relatively new regeneration protocols have been developed that aim to increase yield potential by incorporating resistance to disease and stress as well as safety by circumventing interspecific crossing barriers in rice field.

**NUTRITIONAL VALUE**

Palmitic and stearic acids are the main principle fatty acids found with concentrations ranging from 8.1-17.3% and 6.1-10.5% respectively. High content of essential monounsaturated fat linoleic acid ie. 50.6-60.1% in the oil of seed acts as a principle component for restorative activities. Fat profile of unsaturated fatty acids exposes that the class of linoleicoleic acid bear a close resembalance to few other vegetable oil. Seeds contain 13.19g of protein, 18.59g of fat, 4.91g of moisture and 2mg of ash per 100g. Mineral present in the seeds contain 569mg Ca, 465mg of K, 210mg of Mg , 30.0mg of P, 11.9mg of Na, 11.6mg of Fe, 5.1mg of Cu and 1.1mg of Zn . [4][5]

**VERNACULAR NAMES IN INDIA**

1. Tamil - Paedikari Attutummatti

2. English - Colocynth

3. Sanskrit - Indravaruni

4. Hindi - Indrayan , Badi indrayan

5. Bengali - Makhal

6. Gujarati - Indrayan

7. Marathi - Kadu-indravani

8. Telugu - Erri-Puchcha , Chittipaapara

9. Malayalam - Paikummatti , Kattuvellari

10. Punjabi - Ghurunba

11. Kannada - Daasamekke , Balibandrakshi

**NUTRITIONAL PROFILE AND CHEMICAL COMPOSITION**

Although parts of C.Colocynthis are widely incorporated in food as well as in the pharma industry, little nutritional information is publicly available for the global readers. A few variations in the attributes may be found due to differences in agricultural environment conditions and farming techniques used in different countries (Berwal et al. 2022) [14]. The seed components are composed of approximately 23-25% oil (Golden yellow colored), 70% unsaturated fatty acids as well as 51% polysaturated fatty acids (Berwal et al. 2022) [14]. The moisture content of the ripe fruit is very high, accounting for even more than 90% of the 4.91g/100g, and protein and ash were 13.19g/100g and 2.00g/100g, respectively (Banjo et al. 2021 )[13]. Nutritional profile, fatty acids content and the volatile components of different parts of bitter apple are shown in Table 1. Citrullus colocynthis is high in found are glutamic acid and arginine, recognized with concentrations of 19.8g/100g and 15.9g/100g of protein, respectively. Aspartic acid, serine, glycine, and glutamic acid were among the other amino acids found in protein ( Hussain et al. 2014 )[15]. Minerals are important micronutrients that the body requires to function ordinarily. Each one of the minerals is very well recognized for its advantageous properties in sustaining electrolytic fluids balance and also contributing to the alkalization of the body ( Banjo et al. 2021 )[13]. C.Colocynthis fruits and seeds contain a wide variety of micronutrients that may be beneficial to the consumers. The major minerals found in the seed are potassium and calcium, which have concentration levels of 569mg/100g and 465mg/100g of seeds, respectively ( Hussain et al.2014 )[15]. The seeds are also high in magnesium and phosphorus. Iron and zinc levels are low in comparison to the other micronutrients[13-15].

**Table: 1** Nutrional and fatty acid composition of different parts of Bitter apple

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **S.No** | **Name of Constituents** | **Parts of plant** | **amount** | **References** |
| 1 | **Proximate composition**  Ash (%)  Moisture (%)  Oil content(%)  Fat (%)  Protein (%)  Crude fibres (%)  Starch (%)  Carbohydrate (%) | Seed  Seed  Fruit  Fruit  Seed  Seed  Fruit (mature)  Seed  Seed  Seed  Fruit  Seed  Seed  Fruit  Fruit (mature)  Seed  Seed  Fruit  Fruit | 2.00  2.23  3.08  4.00  4.91  6.43  90.00  28.50  26.60  18.59  3.15  13.19  13.99  24.37  30.00  46.73  1.33  10.88  10.00 | Banjo et al. 2021  Riaz et al.2015  Ogundele et al. 2012  National research council 2006  Banjo et al. 2021  Riaz et al. 2015  National research council 2006  Riaz et al 2015  Banjo et al . 2021  Banjo et al. 2021  Ogundele et al. 2012  Banjo et al . 2021  Riaz et al. 2015  Ogundele et al. 2012  National research council 2006  Riaz et al.2015  Riaz et al.2015  Ogundele et al. 2012  National research council 2006 |
| **2** | **Fatty acids and amino acid profile**  Oleic acid (by wt.% of seed)  Linoleic acid (by wt. % of seed)  Glutamic acid ( % of protein )  Arginin (% of protein )  Palmitic acid (by wt.% of seed)  Stearic acid (by wt.%of seed)  Lignans (%)  Linolenic acid (%) | Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil  Seed oil | 18.02  33.66  50.31  50.60-60.10  54.70  19.80  15.90  8.1-17.30  4.30  12.41  6.10-10.50  15.15  1.83  0.012  2.15 | Berwal et al.2022  Riaz et al. 2015  Berwal et al.2022  Bhasin et al. 2020  Riaz et al.2015  Bhasin et al. 2020  Bhasin et al. 2020  Bhasin et al. 2020  Riaz et al. 2015  Berwal et al. 2022  Bhasin et al. 2020  Berwal et al. 2022  Riaz et al.2015  Berwal et al.2022  Riaz et al.2015 |
| **3** | **Minerals**  Calcium (%)  Potassium (%)  Magnesium (%)  Copper (%)  Sodium (%)  Zinc (%)  Iron (%)  Oryzanol (%) | Seed  Seed residue  Seed  Seed residue  Seed  Seed  Seed  Seed  Seed  Seed residue  Seed oil | 0.057  0.013  0.047  0.012  0.210  0.005  0.012  0.001  0.012  0.004  0.066 | Bhasin et al.2020  Riaz et al.2015  Bhasin et al.2020  Riaz et al.2015  Sadou et al.2007  Sadou et al.2007  Sadou et al.2007  Sadou et al.2007  Banjo et al.2021  Riaz et al.2015  Berwal et al.2022 |
| **4** | **Bioactive compounds and antioxidant activity**  Total phenolic content (mg/100g of oil gallic acid Eq.)  Total flavonoids content (mg/100g of oil catechin Eq.)  Oryzanol (%)  Lignans (%)  Carotenoids (%) | Seed oil  Seed oil  Seed oil  Seed oil  Seed oil | 5.39-6.12  938.0-956.0  0.066-0.069  0.012-0.014  0.008-0.01 | Berwal et al.2022  Berwal et al.2022  Berwal et al.2022  Berwal et al.2022  Berwal et al.2022[6,7,8,9,13,14] |

**AYURVEDA AND SIDDHA ACTION**

As per Ayurveda and Siddha system of medicine Citrullus Colocynthis is

* Tikta-rasam
* Ushna veerayam
* Katu vipakam
* Purgative
* Diuretics
* Lagu
* Kaphaharam
* Puerperal disorder
* Abortifacient
* Ascites
* Dropsy oil from seed used in hair growth and maladu.

**CHEMICAL CONSTITUENTS**

Various bioactive compounds of fruit have been documented in the literature. They are arranged as alkaloids, flavonoids, carbohydrates, glycosides, fatty acids and essential oils. Cucurbitacins have been documented as the major constituents of citrullus colocynthis fruits [16].



**Fig:6** (Chemical constituents present in citrullus colocynthis)

**Cucurbitacins**

These are a group of bitter-tasting and extremely oxygenated, chiefly tetracyclic and triterpenic plant materials derived from the cucurbitane moiety. These are not expressed as steroidal due to the relocation of methyl group from C-10 to C-9 (Fig. A & B). The cucurbitaceae family [17].

**Glycosides, Polyphenols and Flavonoids**

Two cucurbitacin glycosides i.e., 2-O-β-D-glucopyranosyl cucurbitacin I and 2-O-β-D-glucopyranosyl cucurbitacin L and three flavonoids glycosides i.e., isosaponarin (Fig. C), isovitexin (Fig. E) were extricated from Citrullus colocynthis fruits. Polyphenols are a set of natural compounds that act as free-radical terminators and show anti-oxidant activity. Flavonoids are the secondary metabolites that show anti-oxidant and radical- sccavenging activities [18,19].

**BITTER CUCUMBER USES**

The bitter apple root is used for diabetes, high cholesterol, constipation and skin problems. This is ready to use powder pack and comes with 2-year expiry, take 1-3 grams twice a day with lukewarm water or as recommended or consult a doctor before use. Some other uses include:

**As a food ingredient:** Citrulluscolocynthis root powder is used in some culinary cultures as a food ingredient to add a bitter flavour to dishes.

**As a traditional remedy:** In traditional medicine, the root powder is used as a natural remedy, the root powder is used as a natural remedy for digestive and parasitic issues.

**BITTER APPLE HEALTH BENEFITS**

Citrullus colocynthis root has anti-diabetic, anti-oxidant, anti-inflammatory and anti-bacterial properties. It controls blood sugar and intestinal parasites and gives relief from constipation and stomachache.

**Digestive support:** Citrulluscolocynthis root powder is commonly used as a natural remedy for digestive issues, such as constipation, indigestion and diarrhea.

**Anti-inflammatory properties:** The root powder has been shown to have anti-inflammatory properties, which may help reduce swelling and pain in condition like rheumatoid arthritis.

**Anti-parasitic:** The root powder has been used traditionally as a natural remedy to treat parasitic infections, including tapeworms and other intestinal parasites.

**TRADITIONAL FOOD PRODUCTS OF C.COLOCYNTHIS (L.)**

Conventionally egusi seeds are used in many dishes. Ogiri is a greasy paste produced from the kernels of melon seeds. It is well-known in west Africa, notably in Nigeria as a low-cost fermented soup seasoning or taste enhancer. Ogiri has been made from a variety of seed kernels, but egusi melon kernels are the most common (chukwu et al. 2018) [20]. Robo is particularly famous among Nigeria’s Yoruba people. Robo contains a lot of protein as it is produced from the defatted cake of the fruit. This helps to explain why certain Nigerians like Robo and corn cereal which is also called ogiri cereal. Robo is quite comparable to the groundnut cake known as ‘kuli kuli’ in Northern Nigeria (Akinoso & Are 2018) [21]. Egusi pudding is popular among Cameroonians residing in west Africa. It is typically offered during social gatherings. The ingredients used to make egusi pudding differs, but the most common include beef, chicken, eggs, and other seasonings (Giwa & Akanbi 2020) [22].

**FUNCTIONAL AND BIOACTIVE COMPOUNDS**

**Phenolic acids and flavonoids**

Penolic compounds constitue one of the most numerous and ubiquitous groups of plant metabolites. These compounds possess biological properties which mainly include anti-aging, anti-antherosclerosis, cardio-vascular safeguards, vascular endothelium function improvement, angiogenesis inhibition, and cell proliferation (kim et al.2022) [23]. Flavonoids are phenolic compounds (typically hydroxylated) that are produced by plants in reaction to infection by microbes. They have been reported to have in-vitro anti-microbial properties against a variety of microorganisms ( omojate godstime et al.2014 )[24]. They are also potent antioxidants with cytotoxic activity. Such compounds tend to play critical roles in infectious agent as well as in predator defense, and also in physiological mechanisms such as seed development and stunted growth. Flavonoids are beneficial to humans because of the antioxidant properties and radical scavenging properties, and they also have potential anti-cancer properties. These compounds have the potential to be beneficial in disease resistance (karak.2019) [25]. These substances have the potential to be beneficial in resistance to different diseases (Ahmed et al..2019) [26].

**Curcubitacin**

Natural antioxidants are triterpenoid chemicals that are well known for their bitter flavour and toxic effects (Hussain et al..2014) [15]. Curcubitacins play an essential part in drug development, particularly in the development of chemotherapeutic agents, due to their anti-cancerous properties. The studies conducted on citrullus colocynthis agents shows the presence of Cucurbitacin L, Colocynthosides A, and cucurbitacin B. They were found in different part such as seeds and fruits (rezai et al..2017) [27]. The primary cucurbitacin type demonstrates antiallergic properties. Different studies reveal the configuration relationship of cucurbitacin and its derivatives, which have been proficient in electrochemical reaction on cell materials or gene products (Rezai et al..2017) [27].

**Alkaloids**

Alkaloids have always been recognized to play functions such as biochemical and structural in biological organisms. Tis substance has a defensive function in living creatures and has been used in healthcare, particularly steroidal alkaloids, which also make up the majority of beneficial substances (Saxena et al. 2013) [28]. Furthermore, phyto-constituents with effective trypanocidal interaction were reported to produce active ingredients, favonoids, phenolics, etc. Satyavani et al. (2011) reported that C. colocynthis contains a high concentration of alkaloids. A study reported presence of secluded choline and a total of two un-identifed naturally occurring substances from bitter apple fruit pulp. Alkaloids are supposed to play metabolic and developmental functions in life processes. This substance seems to have a defensive function in animals and has been utilized in medical science, example steroidal alkaloids (Saxena et al. 2013) [28].

**Saponins**

The extracts of the plant were found to have saponins that are recognized to provide an anti-inflammatory effect. They consist of triterpene and sterol glycosides which are utilized as expectorants and emulsifiers. As a result, saponin, like a carbohydrate derivative, could be steroids or tri-terpenoids (Khan et al. 2012) [29]. They are produced by combining phenylpropanoids as well as precursors of acetate-derivatives. Innumerable studies have highlighted the effectiveness and participation of steroidal saponins in community pharmacies (Egbuna et al. 2020) [30]. The application of different parts of the bitter apple plants, their bioactive compounds, and the mode of action are mentioned. Furthermore, saponin is utilized in the pharmaceutical industries as well as in medicines due to its frothing capacity and foamy impact. Saponin has been used in medicine since ancient times and is one of the widely accepted bioactive components in cytotoxicity (Abdulridha et al. 2020) [31].

**ETHNOBOTANICAL IMPORTANCES**

Most of the tribal areas and rural communities use entire plant but seeds are used to cure Bowel complaints Blackness of grey hair and Malaria. Fruits are used to reduce stomach ache, Dropsy timely and easy delivery Hepatitis, Snake poison. Roots are applied in the form of paste to enlarge the abdomen and to cure Rheumatism. More knowledge about ethnobotanical importance of the various plant parts has been obtained [32-42].

**DISTRIBUTION OF CITRULLUS COLOCYNTHIS**

The Citrullus colocynthis Wild and cultivated also found throughout India and Ceylon. It is also indigenous in Arabia, tropical Africa, the Mediterranean region, and West Asia.

**PHYTOCHEMICAL STUDIES**

Various important chemical constituents are elucidated from entire plant (root, stem, leaves, fruit and seeds) are documented in literature imparting medicinal value to the genus are carbohydrates, proteins, separated, amino acids, alkaloids, flavonoids, terpenoids. Fruits are the main source of drugs. Citrullus colocynthis have proved to have several active chemical constituents like colocynthin, colocynthetin, cucurbitacins, á-elaterin, cucurbitacines, cucurbitacin glycosides, flavonoids and flavone glycosides. The well-known bioactive compounds of fruit are cucurbitacins; cucurbitacins E (richly found from pulp), Phenolics, Flavonoids, Fatty Acids, Alcoholic and Ketonic alkyl chains. These metabolites like phenols, tannins and flavonoids play very important role in defense mechanism against diseases caused by various bacteria and fungi.

The major bioactiveor principal compounds imparting medicinal values are group of Cucurbitacins i.e cucurbitacin (A, B, C, D, E, J and L) with some other compounds like alkaloids, terpenoids, tannins, saponins, anthranol, caffeic acid, cardic glycoloids. The active compounds such as saponins, sterols, steroids, terpene, flavonoids, tannins and alkaloids were reported from leaves, fruits and roots. Alkaloids were found in all plant except roots, while flavonoids were only reported in seeds; steroids were present in all plant parts, while Gallic acid, tannins and cumarins were only reported in leaves. The presence of alkaloids, steroids glycosides and flavonoids were detected from seeds.

Cucurbitacins, the active compound of family was divided into 12 different classes. Cucurbitacin E was richly isolated from fruit pulp, while from fruit colocynthoside A and colocynthoside B were isolated. Colocynthoside compounds were isolated from methanolic extract of fruits. Various compounds of cucurbitacin i.e d, e, f, g and some flavonoids glucosides such as isovitixin, isorintin and isosapanorin were reported from fruit extracts (butanol). Among the all compounds extracted from fruits, cucurbitacin and the glycosides were highly studied and nearly 20 of these were observed to be very highly oxygenated triterpinoides, Hydromethanolic extract was reported to show the presence of alkaloids, tannins, saponins, flavonoids, unsaturated sterols, terpenes, sterols and steroids from fruits, leaves and roots. The amount of alkaloids, tannins, saponins and flavonoids were found to be in very low quantity from leaves.

The presence of alkaloids, glycosides, terpenoids, tannins, anthraquinol were observed in hexane, ethanol and methanol solvents, while reducing sugars were only present in hexane and ethanol. Flavonoids were only reported in ethanol. Ursolic acids, cucurbitacin E, 2-0-β-D-glycopyranoside, 4-methylqumoline were extracted from methanolic extracts of fruits. The hydromethanolic extracts, ether extract, chloroform methanol (1:1) extract, butanol extract of fruits was reported to isolate 3’0 methyl ether, cucurbitacin glycoside, elatericin B, tetra hydoelatericin B, elaterin dell cucurbitacin E, I and E, while the chloroform extracts of whole plant constitute compounds cucurbitacin E, cucurbitacin I and cucurbitacin L. Phytochemicals viz. carbohydrates, alkaloids, fatty acids, glycosides, flavonoids and essential oils, have been expounded in the fruit of Citrullus colocynthis by various researchers so far.

The most widely reported phytochemical is Cucurbitacins, in the family Cucurbitaceae. The property of cytotoxicity of Cucurbitacins appear to take up an essential part in drug discovery, specifically as anti-cancer drug recovery. Cucurbitacin E (compound a) out of all cucurbitacins was exposed abundantly in the extract of fruit pulp, while other major principle compunds like Colocynthoside A (compound b) and Colocynthoside B (compound c), were elucidated in methanol fruit extracts. Other compounds of Cucurbitacins secluded from butanolic extracts were enlisted as; Cucurbitacin L 2-O-β-D-glucopyranoside (compound d), hexanocucurbitacin I 2-O-β-D glucopyranoside (compound e), cucurbitacin K 2-O-β-D glucopyranoside (compound f) and khekadaengoside E (compound g), cucurbitacin J 2-O-β-D glucopyranoside (compound h), cucurbitacin I 2-O-β-D glucopyranoside (compound i). The butanol fractions of extracts of whole plant parts of methanol reveals the presencertain flavonoid glycosides compounds e.g., isoorientin 30-O-methyl ether (compound j), isovitexin (compound k) and isosaponarin (compound l) along two Cucurbitacin glycosides compounds named as 2-O-β-D-glucopyranosyl cucurbitacin L and 2-O-β -D-glucopyranosyl cucurbitacin L. Similarly, the compounds of flavone glucosides and Cucurbitacin glucosides were isolated from the fruit extracts [43-58].

**MEDICINAL PLANT *Citrullus colocynthis***

Citrullus Colocynthis is perennial herbs normally found wild in the sandy lands of North West, Punjab, Sind and Rajasthan, Central and Southern region of India. Also found native in Arabia, Tropical Africa, West Asia, and the Mediterranean region. The scientific name of this medicinal plant is initially Colocynthis Citrullus but is currently classified as Citrullus colocynthis. Tendrils are simple, 2-3 fits slender and hairy. Leaves are very variable in size. The length of C. colocynthis leaf is 3.8 to 6.3 cm and width are 2.5 cm whereas, the medicinal plant is cultivated in are in large numbers. The Leaf is the pale green colour on the above side and ashy colour on the beneath side; deltoid margin and scab ride on both surfaces with 5-7 lobed are found. Citrullus colocynthis shows the presence of female and male flowers. Fruit are bulbous, slightly depressed; size is 5-7.5 cm in diameter, green in colour, and gets white glabrous when ripe. The fruit has dry, spongy and bitter pulp. The size of seeds is 4-6 mm long and pale brown.

**PHARMACOLOGICAL ACTIVITIES**

**Anti-inflammatory Activity**

Belsem Marzouk and et al study aqueous extracts C.colocynthis fruit and seed at immature state for Anti-inflammatory activity using the carrageenan induced paw edema assay in rats. The best anti-inflammatory activities were obtained with immature fruits from south Tunisia. Could be a potential useful product suitable for further evaluation for inflammatory diseases [59].

**Anti-oxidant Activity**

Extracts isolated from the fruits of Citrullus colocynthis sch as Flavonoids, isovitexin, isosaponarin and isoorientin 3’-O-methyl ether revealed as significant antioxidants. The Anti-oxidant and free radical scavenging ability of the methanolic extract of the fruit of Citrullus colocynthis was evaluated. The highest ability would be found at the concentration of 2500mg/ml. various seed extracts of citrullus colocynthis such as a defatted aqueous extract (E20), a crude aqueous extract (E1), an ethyl acetate extract (EA), a hydromethanolic extract (HM) and n-butanol extract (n-B) were examined in a 1,1-diphenyl-2-picrylhydrazyl assay at a concentration of 2000µg/ml. The decreasing percentage of 88.8% with EA, 74.5% with HM and 66.2% with E1 were noted, with a parallel IC50 of 350, 580 and 500µg/ml subsequently as correlated to 1.1µg/ml for ascorbic acid. The methanolic seed extract of Citrullus colocynthis was studied for the antioxidant activity spectrophotometrically by using 1,1-diphenyl-2-picryl hydrazyl and H2O2 free radical scavenging method. The extract exhibited highest percentage inhibition of 79.4 and 72.4% by 1,1-diphenyl-2-picryl hydrazyl and H2O2 method subsequently at 300µg/ml. Methanolic extract of Citrullus colocynthis fruits (MECC) inhibited the highest percentage of DPPH radicals and nitric oxide radical scavenging model in In vitro antioxidant studies, i.e., 62% and 56% at 800µg/ml, the extract showed the dose-dependent antioxidant activity in comparison of ascorbic acid [60-64].

**Anti-microbial Activity**

The silver Nanoparticles (SNPs) using aqueous extract (AEs) of Citullus colocynthis were investigated against different bacterial species; Staphylococcus epidermidis, Escherichia coli, Pseudomonas, Staphylococcus aureus, Klebsiella pneumonia, Streptococcus pyogenes; antifungal activity against Geotricum candidum, Aspergillus fumigatus, Candia albicans and Trichophyton mentagrophytes, with inhibition zones ranging from 15.1±0.44 to 25.2 ± 0.37mm respectively. The results showed that SNPs/C.clocynthis roots AEs had strongest antimicrobial activity causing 70%, 73% and 75% reduction of the Cytopathic effect (CPE). The antibacterial potentialities of crude ethanolic extracts Citrullus colocynthis were examined for against Gram positive and Gram negative bacilli. Ethanolic extracts of fruits, leaves, stems and roots were established active results against Gram-positive bacilli, viz., Bacilus pumilus and Staphylococcus aureus, whereas fruit and root extracts in higher potency gave positive results against Gram-positive bacilli viz., Escherichia coli and Pseudomonas aeruginosa showed no reaction. The research concluded that active responses against the various strains of bacteria may be because of flavonoid, carbohydrates, tannin and glycosides that are reported. In vitro antibacterial and anticandidal activity of aqueous and diluted acetone extracts of citrullus colocynthis schard had been examined against the Gram-negative and Gram-positive bacteria ( Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Enterococcus faecalis) and various candida spp. ( Candida glabrata, Candida kreusei ). MIC and MBC/MFC were determined for plant organs at different maturation stages. The results showed the highest MICs and MBCs/MFCs from the fruit aqueous extracts Escherichia coli and Pseudomonas aeruginosa ) and the lowest activity from the root extracts[65-67].

**Anti-cancer Activity**

In human breast cancer cell growth, the anti-proliferative impact of cucurbitacin glycosides derived from Citrullus colocynthis leaves was studied. Cucurbitacin B/E glycosides were extracted from the leaves and separated from the extract[68].

**Anti-oxidant, Anti-inflammatory / Analgesic or Anti-proliferative**

Saba AB and et al isolated cucurbitacins are triterpenoids steroids. It is efficient anti-oxidant and this property lies in their ability to scavenge free-radicals such as hydroxyl radical, superoxide anions and singlet oxygen. This broad-spectrum radical scavenging capacity surpasses what had been reported for other natural antioxidants such as grape-seed extract, wheat, alfalfa and ginkgo biloba extracts. Reports also show that cucurbitacins adequately inhibit lipid peroxidation and oxidation [69].

**Anti-diabetic activity**

Citrullus colocynthis was used to possess anti-diabetic effect in rate of 50mg/kg and 100mg/kg for 28 days. Haematological and Biochemical estimations were executed at the end of experiment i.e on 29th day by means of standard kits. The results showed that Citrullus colocynthis could be used for safe an anti-diabetic remedy. The petroleum ether extract of Citrullus colocynthis fruits was usec for the study on lowering the blood glucose levels and thiobarbituric acid reactive substances (TBARS) in Streptozotocin induced Diabetic albino rats. The extract showed a significant decrease in blood glucose level in diabetic rats as well as it significantly reduces TBARS levels when compared to Glibenclamide (0.5mg/kg). A significant decrease in HbA1c and fasting blood glucose levels was found in the patients of type II diabetes when they were treated with Citrullus colocynthis (L.) Schrad fruit for 2 months. LDL, HDL, triglyceride, fasting blood glucose, HbA1c, total cholesterol, aspartate transaminase, urea and creatinine levels were checked at regular interval of time.

The crude aqueous, ethyl acetate, defatted aqueous, H2O-methanol, n-butanol extract and H2O-methanol extracts of the seeds of Citrullus colocynthis had been examineded in glucose stimulate insulin discharge from pancreatic islet of rats. Out of these, various extracts exhibited a positive insulin tropic response as compared to 8.3mm D-glucose. Haematological and biochemical estimations were done on rats treated with Citrullus colocynthis at the dose of 50 and 100 mg/kg for 28 days and the results showed that the plant is safe as a diabetes using root of Citrullus colocynthis was evaluated in rats.

Aqueous extract exhibited significant decrease in blood sugar level (58.70%) in comparision of chloroform (34.72%) and ethanol extracts (36.60%) (p<0.01). The liver hexokinase and gluconeogenic enzymes such as glucose-6-phosphatase and fructose 1, 6-bisphosphatase of control and alloxan-diabetic rats was treated with the leaf suspension of Citrullus colocynthis. The study revealed in momentous decrease in blood glucose level (from 381±34 to 105±35 mg/dl), a reduction in the activities of glucose-6 phosphatase, glycosylated haemoglobin and fructose 1, 6-bisphosphatase and a raise in the action of liver hexokinase. The research concluded another support to the anti-diabetic effect exhibited by Citrullus colocynthis[70-75].

**Anti-bacterial and Anti-candidal**

Marzouk B and et al assess in vitro anti-bacterial and anti-candidal activity of aqueous and diluted acetone extracts of Citrullus colocynthis Schrad. MIC and MBC/MFC were determined for plant organs at different maturation stages. Aqueous and diluted acetone extracts (from the plants root, stem, leaves and three maturation stages of its fruit and seed) were screened for activity against Gram-negative and Gram-positive bacteria (Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Entercoccus faecalis) and various candida kreusei). RESULT: All extracts (MIC 0.10mg/ml against Candida albicans and Candida glabrata, 0.20mg/ml against Escherichia coli and pseudomonas aeruginosa), lowest activity from the root extracts[76].

**Effect of Hair Growth**

Extracts of citrullus colocynthis were tested for the treatment of comparison of minoxidil in rats. The extracts of plant integrated into oily ointment base and 2% monoxidil, both were applied topically on shaved disrobed skin. The time period requisite for initation of growth as well as completion of cycle was recorded. The treatment showed positive results as it brings a greater number of follicles (>70%) to anagenic stage than minoxidil (67%)[77].

**Anti-fertility**

Chaturvedi M and et al screened 50% ethanol extract of Citrullus colocynthis Schrad in male albino rats for evaluation of anti-fertility effects. The animals were divided into five groups: group A was a vehicle-treated control group; treatment group B, C and D received 100mg/kg/day C. Colocynthis extract for periods of 20, 40 and 60 days, respectively and group E animals received the extracts at 100mg/kg/day for 60 days followed by 60 days of recovery. For androgenicity evaluation of the extract, the animals were divided into four groups: group F animals were castrated 30 days before the experiments, followed by administration of fruit extract (100mg/kg/day p.o.), testosterone propionate (0.01mg/rat/alternate day s.c.) and the fruit extract along with testosterone propionate, respectively, for 30 days. Significantly reduced cauda epididymis sperm motility and density, number of pups, fertility and circulatory levels of testosterone were observed in all treatment groups. The weights of testes, epididymis, seminal vesicle and prostate were significantly decreased in group B, C and D. the weight of all organs in the different groups of the androgenicity study were markedly decreased in group A, in group G when compared with group F, and in group I when compared with group H and increased in group F.

The serum testosterone levels also showed a similar pattern. The concentration of testicular cholesterol was significantly elevated, while protein, sialic acid and alkaline phosphatase concentration decreased. The histo-architecture of the testes showed degenerative changes in the seminiferous epithelium, arrest of spermatogenesis at the secondary spermatocyte stage, cytolysis and the lumen filled with eosinophilic material. Histometric parameters expect sertoil cell nuclear area and number of round spermatids showed marked alterations. All altered parameters restored to normal in group E. No change were observed in body weight, litter size, haematology and serum biochemistry. In conclusion, a 50% ethanol extract of C.Colocynthis showed an anti-androgenic nature, thereby reduced reversible infertility nature, thereby reduced reversible infertility in male albino rats[78].

**Table 2: Chemical content of citrullus colocynthis**

|  |  |  |
| --- | --- | --- |
| **S.No** | **Part** | **Chemical content (reported/investigated)** |
| 1 | Seed | 1. Fatty acid like stearic, Myristic, Palmitic, Oleic, Linoleic, Linolenic acid. 2. Protein 8.25% and rich content rich in lysine, leucin and sulfo amino acid like methionine 3. Vitamin B1, B2 and Niacin 4. Mineral like Ca, Mg, K, Mn, Fe, P and Zn |
| 2 | Aerial part and fruit | Flavonoid glycoside quercetin, Flavone-3-glycoside viz iso- vitexin, iso-orentine and iso-orentine-3-methyl ether. |
| 3 | Fruit | 1. Cucurbitacin type triterpen glycoside viz colocynthoside A & B. 2. Cucurbitane type triterpen glycoside viz cucurbitacin E 2-O-beta-D-glycoside and its aglycone Cucurbitacin E. 3. 2-O-beta-D-glycopyransoyl-16alpha-20R-dihyroxy-cucurbita-1,5,23E,25(26)-teraen-3,11,22-trione. 4. 2-O-beta-D-glcopyranosyl-cucurbitacin B and 2, 25-di-O-beta-D-glycopyranosyl cucurbitacin L. |

**Hypolipidemic**

Rahbar AR and et al investigate the hypolipidemic effect of Citrullus colocynthis beyond the hypoglycemic impact on human. One hundred dislipidemic patients were randomly divided into two groups namely treated (n=50) group. The subjects were treated daily by powered seeds of citrullus colocynthis (300mg) and placebo for 6 weeks. The serums, TG, Chol, LDL-C, HDL-C, SGOT and SGPT were measured with enzymatic methods at the beginning and the end of the project. The significance of differences within these groups was calculated by paired T-test and by analysis of covariance between them. There were significant differences within and between treated and placebo groups during our treatment and placebo groups during our treatment in TG and in cholesterol after intervention (p<0.05). A daily intake of 300mg/day (-1) of powered seeds of citrullus colocynthis can lower the triglyceride and cholesterol concentration significantly in nondiabetic hyperlipidemic patients[79].

**Growth inhibitory activity on breast cancer cells**

Grossman S and et al study the effects of Cucurbitacin glycosides extracted from Citrullus colocynthis leaves on human breast cancer cell growth. Leaves were extracted, resulting in the identification of cucurbitacin B/E glycosides. The Cucurbitacin glycoside combination (1:1) inhibited growth of ER(-) MDA-MB-231 human breast cancer cell lines. Cell-cycle analysis showed that treatment with isolated cucurbitacin glycoside combination resulted in accumulation of cells at the G(2)/M phase of the cells cycle. Treated cells showed rapid reduction in the level of the key protein complex necessary to the regulation of G(2) exit and initiation of mitosis, namely the p34 (CDC2)/cyclin B1 complex. Cucurbitacin glucoside treatment also caused changes in the overall cell morphology from an elongated form to around-shaped cell, which indicates that cucurbitacin treatment caused impairment of actin filament organization.

This profound morphological change might also influences intracellular signalling by molecules such as PKB, resulting in inhibition in the transmission of survival signals. Reduction in PKB phosphorylation and inhibition of surviving, an anti-apoptosis family member, was observed. The treatment caused elevation in p-STAT3 and in p21(WAF), proven to be STAT3 positive target in absences of survival signals. Cucurbitacin glycoside treatment also induced apoptosis, as measured by Annexin V/propidium iodide staining and by change in mitochemicals memberane potential (DeltaPsi) using a fluorescent dye, JC-1. We suggest that cucurbitacin glycosides exhibit pleiotropic effects on cells, causing both cell cycle arrest and apoptosis. These results suggest that cucurbitacin glycosides might have therapeuticin value against breast cancer cells[80].

**Side Effects and Toxicity**

The study for toxicity of fruit pulp extract of Citrullus colocynthis was performed. Gross phenomenal conclusion found on the 20th day of conception exposed that a high fraction of resorbed embryo, smaller in size and weight as well as lack of coccygeal vertebral column and bones. It could be concluded that the teratogenic effects may be caused by extract of fruit pulp of Citullus colocynthis if given at the initial period of pregnancy. A study had been performed on the rabbits to measure the toxic effects of seed extract and pulp extract of Citrullus colocynthis, all of them were served with 100-200mg/kg/day of either pulp or seed extract. After one month, no animals treated with 200mg/kg/day of pulp extract sustained. Animals treated with less dose of pulp extract showed rigorous abrasions in the liver, small intestine and kidney. However, animals treated with seed extracts showed only minor intestinal effects. It could be concluded that in compare to seed extracts, pulb extracts of plant material can be lethal [81,82].

**Hypoglycemic**

Agarwal V and et al examine the effects of root of C.colocynthis on the biochemical parameters of normal and alloxan-induced diabetic rats. Diabetes mellitus was induced by intraperitoneal (120mg/kg b.w.) injection of alloxan showing blood glucose concentrations of the animals were repeated on 3rd, 5th and 7th day after the start of the experiment. On day 7, blood was collected by cardiac puncture under mild ether anesthesia. Aqueous extracts of roots of Citrullus colocynthis showed significant reduction in blood sugar level (58.70%) when compared with chloroform (34.72%) and ethanol extracts (36.60%) (p<0.01). The aqueous extracts showed improvement in parameters like body weight, serum creatinine, Serum urea and serum protein as well as lipid profile and also restored the serum level of bilirubin total, conjugated bilirubin, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP)[83].

**Mosquito larvicidal Activity**

Rahuman AA and et al assayed Citrullus colocynthis (Linn.) Schrad, for their toxicity against the early fourth instar larvae of culex quinquefasciatus ( Diptera: Culicidae). The larval mortality was observed after 24h exposure. All extracts showed moderate larvicidal effects; however, the highest larval mortality was found in whole plant petroleum ether extract of C.colocynthis. In the present study, bioassay-guided fractionation of petroleum ether extract led to the separation and identification of fatty acids; oleic acid and linoleic acid were isolated and identified as mosquito larvicidal compounds. Oleic and linoleic acids were quite potent against fourth instar larvae of Aedes aegypti L. (LC50 8.80, 18.20 and LC90 35.39, 96.33 ppm), Anopheles stephensi liston (LC50 9.79, 11.49 and LC90 37.42, 47.35 ppm) and culex quinquefasciatus say (LC50 7.66, 27.24 and LC90 30.71, 70.38 ppm). The structure was elucidated from infrared, ultraviolet, 1H-nuclear magnetic resonance, 13C-NMR and mass spectral data[84].

**Larvicidal**

Rahuman AA and et al tested larvicidal activity of crude hexane, ethyl acetate, petroleum ether, acetone and methanol extracts of the leaf of five species of cucurbitaceous plants against the early fourth instar larvae of Aedes aegypti L. and culex quinquefasciatus (say) (Diptera: Culicidae). The larval mortality was observed after 24h of exposure. All extracts showed moderate larvicidal effects; however, the highest larval mortality was found in petroleum ether extract of C.colocynthis, methanol extracts of C. indica, C. sativus, M.charantia and acetone extract of T. angunia against the larvae of A. aegypti (LC50=74.57, 309.46, 492.73, 199.14 and 554.20 ppm) and against C.quinquefasciatus (LC50=88.24, 377.69, 207.61 and 842.34 ppm) respectively. The petroleum ether extract of C.colocynthis and methanol extract of M.charantia were more effective than the other extracts[85].

**CONCLUSION**

This review certainly implies that C.colocynthis is a fruit crop with potential application in the treatment of a variety of metabolic disorders. Although a bitter apple has a dietary supplementation significance, it’s not universally acknowledged. Citrullus colocynthis is reported as having anti-diabetics, anti-inflammatory, anti-microbial, analgesic, anti-oxidant, anti-cancer, anti-fertility activity is the most significant. It can be concluded that fruit extract of C.colocynthis is hepatotoxic and has a toxic effects on the kidney. Efforts must be exerted to identify plants utilized in folk medicine having narrow therapeutic indices as their use is dangerous and should be carefully researched, especially plants used by diabetic patients. The review describes all the necessary phytochemicals, bioactive compounds, and their mode of action for the treatment of various diseases such as cancer, inflammatory and many more diseases.

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