Plumbaginaceae medicinal plant that belongs to the family chitramoolam doctor bush, or leadwort is the popular 'lead', refers to the plant ability to treat lead palsy or the derived from the Latin word Plumbum which means leadwort ayurvedic medicines [4]. According to a reported study, WHO is medicinal system of India and is widely accepted as the most significant herbal plant in the ayurveda effects [3]. The usage of medicinal herbal plants is increasing worldwide [2]. Most people depend upon studies [1]. The usage of medicinal herbal plants is synthesized from herbal plant origin as per reported pharmaceutical industries. 50% of the modern drugs are taken in excessive amount. From the collected data, it is clear that the plant has great potential to cure various diseases and needs more research and development to explore its more pharmacological properties and socio-economic impact.

Keywords- Chitraka, Anticancer, Ayurveda, Rejuvenator, Pharmacological property.

I. INTRODUCTION

Herbal plants play an important role in pharmaceutical industries. 50% of the modern drugs are synthesized from herbal plant origin as per reported studies [1]. The usage of medicinal herbal plants is increasing worldwide [2]. Most people depend upon herbal medicines as they are non-toxic with fewer side effects [3]. According to a reported study, WHO is encouraging developing countries to use herbal or ayurvedic medicines [4].

Plumbago zeylanica commonly called chitraka, chitramooolam doctor bush, or leadwort is the popular medicinal plant that belongs to the family Plumbaginaceae also referred as Plumbago family or leadwort family [5]. The generic name Plumbago is derived from the Latin word Plumbum which means 'lead', refers to the plant ability to treat lead palsy or the ability of plant sap to form lead-colored stains on the skin [6,7] and zeylanica means 'of Ceylon'. The genus Plumbago consists of 3 species named Plumbago indica, Plumbago capensis and Plumbago zeylanica that are distributed in several parts of India. This plant is considered as the multipurpose medicinal herbal plant, which is used in the traditional medicinal systems like Ayurveda and Siddha medicinal system for over 3000 years. The plant is native to southeast Asia and is grown in tropical and subtropical regions up to an altitude of 2000m [8-11]. Traditionally, the roots of this plant are used to cure diseases like headache, body pain, fever, muscular pain, rheumatic diseases, inflammation and also acts as a stimulant digestant, expectorant and laxative [12]. In Ayurveda and Unani medicinal system, it is used to treat diseases like rheumatic pain, sprain, scabies, anemia, dysmenorrhea, carbuncles, leprosy, ulcers, inflammation and elimination of intestinal parasites [13-18]. In India, it is mainly used to cure fever, malaria, dyspepsia, piles, diarrhea and skin diseases [19]. The main active constituent of the PZ plant is Plumbagin found in the root part of the plant. The plant possesses various pharmacological properties like antidiarrheal [20], anti-allergic, insecticidal, antidiabetic [21], hepatoprotective [22], hypolipidemic [23], anti-inflammatory, antitumor [24], antibacterial, antimalarial and antifungal activities [25,26]. Chitraka plant is known by various folk names in different states of India and in other countries as shown in table no. 1. The taxonomical classification of chitraka plant is shown in table no. 2.

Table 1: Vernacular names of Plumbago zeylanica [27]

| Language | Vernacular Name       |
|----------|-----------------------|
| Hindi    | Chitraka, chita, Chitramol, chiti, chitra [28,29,30] |
| Gujarati | Agni / vahini, Chitro, chitra, pitaro, chitruk, chitrakmula [31,32] |
| Kannada  | Chitramula, vahini, Pellichtramool, chitrakmulikula, Bilichitru [33] |
| Malayalam| Chitrakmula / bilichitramul, Thumpo Koduveli, Vellakoduveli, Tumba koduveli |
| Punjabi  | Chitra, Chitruk [34] |
| Bengali  | Chitra, Chita, Chitak, Safaid chitarak |
| Tamil    | Chita, Adigaaradi, Akkini, |

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II. BOTANICAL DESCRIPTION OF PLUMBAGO ZEYLANICA

The Plumbaginaceae family consists of 280 species and 10 genera. It is a rambling sub-scandent perennial dicot herb or designated as a shrub which is grown in shady places [38,39].

**Root:** The roots of *P. zeylanica* are stout, cylindrical, friable, slightly branched or straight unbranched with or without secondary roots have a smooth and uniform texture. It is blackish-red in color, reddish-brown when dry, light yellow colored when fresh, 30cm in length and 6mm in diameter. It has a specific odor and bitter taste [40].

**Stem:** Stem is glabrous, spreading, somewhat woody, terete and striated reaches up to the height of 0.5 - 2m. The bark is thin and brown [41].

**Leaf:** Leaves are simple, elliptical with hairy margins ovate or oblong, dark green alternate with 8cm in length and 3cm in breadth. The petiole is thin, narrow, amplexicaul at the base and dilated into stipule-like auricles.

**Flower:** Flowers are white, inodorous, inbracteate, bisexual, axillary and terminal elongated spikes consist of terminal raceme inflorescence with length 10-25cm. The calyx is tubular densely covered with stalk, sticky glands, white corolla, slender, 5 free stamens with superior ovary, pentagonous, single-celled and one basal ovule [42].

**Fruit:** Fruits are oblong, capsulated, single-seeded, reddish-brown to dark brown with 7.5-8mm in length.

III. GEOGRAPHICAL DISTRIBUTION OF *P. ZEYLANICA*

*Plumbago zeylanica* is native to Southeast Asia and is distributed in tropical and subtropical regions up to an altitude of 2000m. It is found throughout India in the wild state and mostly grown in Bengal, Malay peninsula, Ceylon-tropics of the old world. In India, it is mainly cultivated in districts of Andhra Pradesh, Karnataka, Maharashtra [43].

IV. PHYTOCHEMICAL CONSTITUENTS OF PLUMBAGO ZEYLANICA

*P. zeylanica* contains secondary metabolites which include flavonoids, alkaloids, saponins, glycosides, tannins, steroids, triterpenoids, carbohydrates, coumarins, fixed oil, phenolic compounds, fats, naphthoquinones and proteins [44]. The screening of different parts of PZ plant also revealed the presence of linoleic acid, nonylnonanoate, palmitic acid, stigmasterol acetate, lupeol acetate, lupeol, friedelinol, lupanone, stigmasterol and sitosterone [45,46,47]. The leaves, stem and roots of PZ plant
contain a greater amount of microelements, (Zn, Fe, Mn, Cr and Co) macroelements (Na, K, Ca, Mg) and eight other elements which include Mo, Sb, Bi, Cd, Sr, Pb, Cd and Arsenic [48]. The chemical constituents present in the aerial part of the plant consist of plumbagin, isohinanolone, plumbagic acid, beta-sitosterol, 4-hydroxybenzaldehyde, trans-cinnamic acid, vanillic acid, 2,5-dimethyl-7-hydroxycromon, indole-3-carboxaldehyde [49]. The dichloromethane extract isolated from aerial parts of PZ plant contains beta-sitosterol, beta-sitosteryl-3 beta-glucopyranoside, beta-sitosteryl-3-beta-glucopyranoside-6'-O-palmitate, lupenone, plumbagin, lupeol acetate and trilinolein [50]. The root of the PZ plant contains different bioactive products which include plumbagic acid glucosides (3'-O-beta-glucopyranosyl plumbagic acid and 3'-O-beta-glucopyranosyl plumbagic acid methyl ester) [51] along with five naphthoquinones (plumbagin [52], chitrinanone, [53] maritime, [54] elliptinone and isoshinanolone [55] and five coumarins (seselin, [56] 5-methoxyseselin, [57] suberosin [58], xanthyletin [59] and xanthoxyletin [60]. Naphthoquinones present in PZ plant includes plumbagin, chitrinanone, 3-biplummbvagin, chlorplumbagin, and elliptone. Other compounds present are saponaretin, isoaffinetin, beta-sitosterol, 2-dimethyl-5-hydroxy-6-acetylcromene, zeylanone, campesterol, isozeylanone, plumbaginol, chitanone [61]. The structures of some major phytochemicals are shown in figure no. 2.

V. TRADITIONAL AND MODERN VIEW OF PLUMBAGO ZEYLANICA

a) P. zeylanica in Ayurveda

Ayurveda means the science of life that provides medicines to a large section of our population. Chitraka plant is considered as an effective herbal drug in Ayurveda medicinal system. All the parts of the plant are used to treat various diseases but the roots of Chitraka plant show highest activity in treating various ailments and disorders [62]. It increases Pitta dosha and alleviates Kapha and Vata. Ayurveda, an indigenous system of medicine has characterized chitraka as tumor –negating and anti-dyspepsia. In Charaka Samhita, it is categorized as an appetizer, anti-saturative, anti-anorexic, pain reliever and anti-hemorrhoid [63]. The rasapanchak (properties) of Chitraka plant are shown in table no. 3.

Root: In Ayurveda, root and root bark has been used to treat dysentery, intestinal troubles, leukoderma, inflammation, piles, bronchitis, itching, disease of the liver, tridosha. Ascites. Milk juice of root bark is applied to ulcers and scabies [64]. Roots act as an abortifacient, vesicant, antidiarrheal, appetizing, sudorific, laxative, expectorant, alexipharmic, thermogenic, antiatherogenic, cardiotonic, neuroprotective, nervous stimulant, diuretic, caustic, antiseptic, antiperiodic, narcotic, rubefacient, aphrodisiac, alternative or restorative (Rasayana or rejuvenator) [65,66]. It is also helpful in the treatment of anasarca, piles, leprosy, anemia, ringworm, scabies, jaundice, urinary calculi, migraine, internal abscesses, seminal weakness, insanity, vaginal discharge (cures menstrual disorders and post-partum discharge), dyspepsia, epilepsy, hysteria, obesity, nervous and rheumatic infections, indolent ulcer, asthma, cough, colic, helminthiasis, elephantiasis, impotency, laryngitis, hepatosplenomegaly [67].

Leaves: The leaves of P. zeylanica plant are used to cure infections and the digestive problem like dysentery and diarrhea. The paste of chitraka leaves is applied over painful rheumatic areas and chronic or itchy skin problems. The flower and fruits of the plant act as digestants. The decoction of the seed is used to decrease muscular pain [67].

Formulations of Chitraka: Pippalyadya churna made from chitraka along with other herbal ingredients helps to promote agni (power of digestion) and eliminates vayu (flatus) from koshta (gastrointestinal tract). Chitrakadya gutika (stimulates the power of digestion and metabolism), Kshirasatpalaka grita in which chitrak is the main ingredient used to treat Kapha, gulma (phantom tumor), sprue syndrome, anemia, splenic disorders and fever. Other formulations include Eldi grita, chitrakadi taila, chitrakavati, chitra katha, chitraka rasayana, chitraka swarasam, chitraka kalkam, chitraka hamam, panchakola, Varemadi, Mushkakadi, Amalakyadi, Shadushana, Trimada, Shaddharana yoga, Drakshasava, Tejovatyadi grita, chitrak swarasam, chitrak swarasam, chitrak swarasam, chitrak avaleha, Chavikadi ghrita, Tejovatyadi ghrita.
Figure 2: Chemical structures of some major phytochemicals of *P. zeylanica* plant.

Table 3: Rasapanchak (properties) of *P. zeylanica*

| Veerya / Potency | Ushna / hot |
|------------------|-------------|
| Vipak / Metabolic property | Katu / bitter |
| Guna / Physical property | Laghu / light, Ruksha / dry, Tikshna / astringent |
| Rasa / Taste | Katu / bitter |

Karma / Action and Properties of *P. zeylanica*

Deepana: It acts as an appetite stimulant.
Pachana: It is used to treat digestive problems
Pittasaraaka: It increases Pitta dosha.
Arshoghana: It is used to cure piles disease.
Grahi: It absorbs excessive fluid in intestine and binds stool.
Krimighna: It helps in treating ringworm.
Kushahara: It alleviates skin diseases.
Raktapittaprakopaka: It is useful in hemorrhagic treatment.
Kaphaghna: It helps in removing Phlegm.

Kanthya: It is beneficial for the throat and voice.
Garbhasravakara: It acts as an abortifacient agent.
Garbhashaya Sankochak: It helps in contracting the uterus.
Swedajanana: It induces sweating.
Jwaraghna: It is used to reduce fever.
Shoolahara: It helps to alleviate pain.
Shothahara: It acts as an anti-inflammatory agent.
Lekhna: It is useful in reducing fat and carries anti-obesity property.
Vajikarana: It is useful in promoting reproductive health and acts as an aphrodisiac agent.
Visphotajanana: It acts as a Vesicant.
Uttejaka: It is used to stimulate nerves.
Madak: It helps in the intoxication process.
Katupaushtika: It is used as a bitter tonic.
Rasayana: It is used as a rejuvenator or Antiaging drug.
Triptighna: It acts as an anti-saturative agent.
Stanya sodhak: It is used as lactode purant.
Sukra sodhaka: It increases the sperm count and its viability.
Adulteration is the major issue in today’s scenario, which is faced by the Global herbal market. It is the main disadvantage in the promotion of herbal drugs and that's why people have lost faith in these medicines [73,74,75,76]. One of the most used practices is Species adulteration. In the herbal drug market species, adulteration has been suspected for quite a while [77]. It has adverse impacts on consumer health [78]. One of the most popular incidents of species adulteration is from China when kidney failure of more than 100 women occurred due to adulteration of species i.e. roots of Stephania tetrandra, which is an anti-inflammatory drug [79]. Many other practices are incorporated in the trade market of herbal drugs in modern times, which are directly or indirectly degrading the quality of herbal medicines. One of them is the use of artificially manufactured material that looks like the original drug. This is the most common practice of adulteration in the case of expensive herbal drugs [80,81]. Due to the presence of several adulterants, the rate of toxicity has increased and also the high cost is the associated factor of adulteration [82].

VI. PHARMACOLOGICAL AND THERAPEUTIC USES

Various experimental and clinical studies were conducted on *P. zeylanica* plant to demonstrate its pharmacological and therapeutic properties. Some of the reported studies of chitraka plant are shown below. A brief view of reported pharmacological studies is shown in table no. 4.

**Anti-microbial:** To identify the anti-microbial activity of *P. zeylanica* plant, the crude alcohol extract of chitraka plant was tested against E-coli and Shigella. It was found that the crude alcoholic extract of chitraka plant inhibits the growth of multi-restraint strains of E. coli and Shigella [83]. Another study was carried out in Bacillus subtilis cultures where the methanolic extract of chitraka plant showed antimicrobial activity [84]. It was also found that theocharic extract of plant showed antimicrobial activity against *Staphylococcus aureus*, *Salmonella typhi*, *Pseudomonas aeruginosa* and Bacillus subtilis where chloroform and acetone showed moderate activity [85]. The crude extract of the leaves of chitraka plant demonstrates an inhibition zone when tested against E. coli, Bacillus cereus, *Staphylococcus aureus* and Candida, which indicates the potential anti-microbial activity of chitraka plant [86].

**Antidiabetic:** Various reported studies stated that the Plumbagin component of Chitraka plant increases the protein and GLUT4 mRNA expression and contributes to the glucose homeostasis when examined against diabetic rats [87]. Another study demonstrated that the ethanolic extract of *P. zeylanica* plant decreased the activity of glucose-6-phosphate and increased the hexokinase activity when administered orally to the streptozotocin-treated diabetic rats at 100mg.200mg/kg dosage [88].

**Anti-inflammatory:** From the reported study, it was found that the hydro-alcoholic extract of the leaf of *P. zeylanica* plant reduces edema, suppresses the NF-kappa B activation in the tumor cells when tested against carrageen an-induced raw paw edema in rats, thus showed anti-inflammatory activity [89,90,91]. The clinical study was conducted on 30 patients taken from OPD and IPD of the National Institute of Ayurveda, Jaipur to detect the anti-inflammatory activity of the chitraka plant [92]. A 4mgs of chitraka churna was given to 15 patients twice a day with lukewarm water for 15 days. Results showed an effective improvement in the pain, swelling, dizziness and tenderness caused due to the inflammation of body parts [93].

**Anticancer:** The chemical constituent named Plumbagin present in the PZ plant possesses anticancer property against various cancer cell lines by restricting cell proliferation, blocking cell cycle and inducing apoptosis of APL cell line NB4 cells [94]. The ethanolic extract of the plant diminishes the elevated level of lipid peroxidation and showed effective anticancer property when tested in Ehrlich Ascites Carcinoma in an animal model [95]. Reported studies revealed that the methanolic extract of the chitraka plant shows anticancer and inhibitory property when tested against MCF-7 and HT-29 [96]. Plumbagin restricts apoptosis in human gastric cancer cells because of its capability to suppress the STAT3 and Akt phosphorylation [97].
**Hepatoprotective activity:** The ethanolic extract of chitraka plant was given orally for 6 weeks in the experimental model i.e. streptozotocin induced diabetic rats. The result showed an increase in hepatic hexokinase activity and decreased hepatic glucose-6-phosphatase, alkaline phosphatase (ALP) serum acid phosphatase (ACP) and lactate dehydrogenase (LDH) [98].

**Hypo-cholesterolemic:** Plumbagin isolated from the root extract of chitraka plant was tested against the hyperlipidemic rabbit. It was found that plumbagin reduces serum cholesterol and LDL by 53% to 86% and 61% to 91% respectively. Also, plumbagin inhibits cholesterol and triglyceride accumulation in the liver and aorta [99]. Another study was conducted in hyperlipidemic rabbits where an ethanolic extract of chitraka plant was given in 500 mg/kg of dosage. Results showed a significant decrease in serum cholesterol, LDL, cholesterol and triglyceride [100].

**Wound healing:** The methanolic and ethanolic extract isolated from *P. zeylanica* roots showed wound healing property when tested against Wistar albino rats [101]. It was found that chitraka plant possesses wound healing property because of the presence of phytoconstituents like flavonoids, alkaloids, terpenoids, saponins and others [102]. Also, chitraka plant helps in balancing wound healing oxidative stress and accelerate wound healing effect [103].

**Larvicidal:** The hexane and chloroform crude extract isolated from chitraka plant showed significant larvicidal activity against *A. gambiae*.i.e. LC50 6.4 and 6.7 mg/ml respectively [104]. Results showed the larvicidal activity of chitraka plant against the second, third and fourth instar larvae stage of *Aedes aegypti*.

**Anti-ulcer:** Falang et al have identified the anti-ulcer activity of aqueous extract of chitraka plant on aspirin and indomethacin induced acute gastric ulceration in albino rats. Later, the ulcer index, ulcer score and percentage protection of the extract with negative and positive control groups were compared and determined. In aspirin-induced gastric mucosal damage, the extract at dosages 25, 50 and 100 ml/kg showed significant results whereas, in indomethacin-induced ulcer, the extract at 50 and 100 mg/kg dosage exhibited statistically significant [105].

**Effect on Central nervous system:** The hydroalcoholic extract of leaf of chitraka plant showed significant CNS depressant activity with the muscle relaxant property [106].

**Antifungal:** The antifungal property of chitraka plant was tested against the pathogenic yeast, *Candida albicans* and dermatophytes, *Epidermophyton floccosum, Microsporum gypseum* and *Trichophyton rubrum*. It was found that the alcoholic extract of chitraka plant showed significant antifungal activity against pathogens and dermatophytes [107].

**Antibacterial:** The aqueous extract (petroleum ether, dichloromethane, methanol, aqueous residue) and alcoholic extract isolated from the root of chitraka plant was investigated for antibacterial activity against *Salmonella gallinarum, E. coli, Proteus vulgaris, Salmonella typhimurium, Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella paratyphi and Shigella dysenteriae*. The result showed significant antibacterial activity against these bacterial species [108].

**Memory enhancing:** The chloroform extract isolated from roots of chitraka plant was tested against scopolamine-induced amnesia for learning and memory of mice. Results showed significant memory enhancing effect and significantly reversed the amnesia induced by scopolamine at 0.4 mg/kg of dosage [109].

**Anti-obesity:** A clinical study was conducted on obese patients of I.P.G.T & R. Hospital at Jamnagar, Gujarat. The intervention of Haridra powder and *P. zeylanica* was given in capsulated form at 500mg and 1gm/4 times for 45 days with a restricted diet schedule. It was found that the chitraka plant showed an effective result in losing weight of the patients than Haridra powder [110].

**Antiviral:** 80% methanolic extract of chitraka plant was tested against Coxsackie Virus B3 (CVB3), influenza A virus and herpes simplex virus type 1 Kupka (HSV-1) using cytopathic effect (CPE) inhibitory assays in HeLa, MDCK and GMK cells respectively. The methanolic extract inhibited CVB3 production and the antiviral activity of most of the compounds was confirmed by a Plaque reduction assay [111].

### Table 4: Reported pharmacological properties of *Plumbago zeylanica*

| S. no. | Extract                  | *Invivo / Invitro model* | Pharmacological property  | References |
|-------|--------------------------|--------------------------|---------------------------|------------|
| 1.    | Alcoholic extract        | *E. coli, Shigella*      | Antimicrobial             | [83]       |
| 2.    | Methanolic extract       | *Bacillus subtilis*      | Antimicrobial             | [84]       |
| 3.    | Ethanol extract, chloroform, acetone extract | *Staphylococcus aureus, Salmonella typhi, Pseudomonas aeruginosa, Bacillus subtilis* | Antimicrobial | [85]       |
| 4.    | Crude extract of leaves  | *E. coli, Bacillus cereus, Staphylococcus aureus, Candida* | Antimicrobial             | [86]       |
| 5.    | Ethanol extract          | Diabetic rat             | Anti-diabetic             | [88]       |
| 6.    | Hydro-alcoholic extract of leaves | Rat model | Anti-inflammatory         | [89][90][91] |
VII. TOXICITY

The excessive use of chitraka plant results in toxic effects. It causes irritation and intoxicant effect. The toxic effects include burning of tongue, throat, stomach and other body parts. It can also cause nausea, vomiting, diarrhea, dysuria, burning micturition, pulse become weak, wrinkled and cold skin [112]. The root of chitraka plant has been reported to have poisonous effect when administered orally and also cause abortion when applied to ostium uteri [113]. From the reported study it was found that the methanolic extract isolated from the root part of chitraka plant showed limited toxicity and didn't show any overt signs of toxicity in the skin when experimented in rabbit. In pregnancy, the utilization of chitraka plant can irritate pelvic organs and ultimately cause abortion.

VIII. CONCLUSION

Plumbago zeylanica is considered as the most important herbal plant and has a specific place in the herbal medicinal system. The usage of the plant is also popularized in Ayurveda and Unani medicinal systems. Because of the presence of bioactive compounds or phytochemicals, the plant is widely accepted as a rejuvenator (Rasayana). Various pharmacological properties of chitraka plant include anti-malarial, anti-obese, anti-diabetic, anti-microbial, anti-ulcer, anti-inflammatory, anti-oxidant and anti-cancer activity. This review aim is to provide comprehensive information on chitraka plant and its utilization in the various medicinal system such as traditional, Ayurveda and Unani medicinal system to treat various ailments and disorders. Also, the plant needs more acceptance in the research area to explore its more pharmacological and therapeutic properties which helps in discoveries of new herbal drugs extracted from chitraka plant to improve the health and well-being of humans.

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