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# A Comprehensive Review on the Anticancerous Activity of *Arka* (*Calotropis procera*)

**Diksha Sharma[1], Munna Lal Prajapati[2], Rajveer Sason[3]**

[1]*Post Graduate Scholar, P.G. Department of Agada Tantra, Rajiv Gandhi Government Post Graduate Ayurvedic College & Hospital, Paprola, Himachal Pradesh, India.*

[2]*Professor, P.G. Department of Agada Tantra, Rajiv Gandhi Government Post Graduate Ayurvedic College & Hospital, Paprola, Himachal Pradesh, India.*

[3]*Assistant Professor, P.G. Department of Agada Tantra, Rajiv Gandhi Government Post Graduate Ayurvedic College & Hospital, Paprola, Himachal Pradesh, India.*

## ABSTRACT

Cancer incidence is increasing both in India and around the world. According to World Health Organization (WHO) estimates for 2019, cancer is the primary or second major cause of death before the age of 70 in 112 of 183 countries, And third or fourth in another 23 countries. The estimated mean relative proportions showed that oral, breast, and cervical cancers remained the leading causes of cancer in India. Medicinal plants include several phytochemicals that are used to synthesize active medicinal compounds, making them extremely important. *Arka* (*Calotropis procera*), a plant revered in traditional medicine for its strong medicinal effects, has been shown to have anticancer potential. *Calotropis procera* is a plant that grows abundantly over the world. *Bhavprakasha* and *Rasatarangini* classify *Calotropis procera* (*Arka*) as an *Ayurvedic Upavisha*. This plant includes numerous phytochemical compounds, including cardenolides, benzoyllineolone, calactin, and calotropagenin. These phytochemicals have been examined and proven beneficial against a variety of diseases. By combining traditional knowledge with modern scientific research, this study intends to highlight *Calotropis procera*'s potential as a source of novel anti-cancer drugs and to guide future research paths in this area. This review highlights numerous in vitro and in vivo investigations on the anticancer efficacy of *Upavisha Arka*.

**Key words:** *Anticancerous Activity, Cancer, Arka, Calotropis procera, Upavisha*

## INTRODUCTION

Cancer is the abnormal multiplication of cells within the human body. The global number of cancer sufferers is growing. Cancer now accounts for one out of every six deaths worldwide, making it more common than HIV/AIDS, TB, and malaria combined. In 2018, 17 million cancer cases were identified worldwide, with 9.5 million cancer deaths, colon cancer being the third highest cause. The global burden of cancer is anticipated to reach 27.5 million new cases and 16.2 million deaths by 2040 as the population grows and ages.[1] Oral, breast, and cervical cancers account for the vast majority of cancer burden in India.[2]

Chemotherapy, surgery, immunotherapy, and other current cancer treatment options are prohibitively expensive and have serious side effects. Medicinal plants are extremely important since they contain a wide variety of components and serve as a source for the manufacture of active medicinal compounds.

*Bhavprakasha* and *Rasatarangini* classify *Calotropis procera* (*Arka*) as an *Ayurvedic Upavisha*. *Calotropis procera* has demonstrated anticancer, cytotoxic, antitumor, and antiproliferative activities.[3,4,5] Many pharmacological activity have also been demonstrated,

**Address for correspondence:**
**Dr. Diksha Sharma**
Post Graduate Scholar, P.G. Department of Agada Tantra, Rajiv Gandhi Government Post Graduate Ayurvedic College & Hospital, Paprola, Himachal Pradesh, India.
**E-mail:** diksha251sharma@gmail.com

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including antihelminthic, hepatoprotective, anti-inflammatory, antidiarrheal, antibacterial, and antinociceptive properties.[6] This plant includes numerous phytochemical compounds, including To cardenolides, benzoyllineolone, calactin, and calotropagenin. These phytochemical ingredients are useful against cancer and other disorders.[7]

To Illustrate the effects of *Calotropis procera*, a number of preclinical investigations have been carried out using a variety of animal models and cell lines, including Hep-2, MCF-7, SNB-78, HCT-15, HCT-8, and HCT-29. *Calotropis procera* has 547 medicinal formulations that are used to treat nearly 58 disorders.[8]

*Calotropis procera* and its phytoconstituents have undergone significant preclinical testing for biological and anticancer effects. *Calotropis procera* is a plant that grows abundantly over the world. This plant has a high concentration of phytochemicals. Searching for new therapeutic agents is a major task for scientists in the current period, and plants are the primary source of these molecules. Screening plants for pharmacological qualities in the goal of discovering a safe and effective drug is critical. A wide range of synthetic chemicals are accessible, but their use is restricted due to environmental risks and negative effects on the human body. *Calotropis procera* is one of the plant-based agents that are safe, effective, and environmentally beneficial.

The current study aims to provide systematic information regarding several *Calotropis procera* extracts and phytochemicals as potential cancer treatments. Thus, this is an attempt to compile all possible references to *Calotropis procera*'s anticancer activity.

## Review of Literature

### Review of *Calotropis procera*[9]

Latin Name: *Calotropis procera* (Ait.) R.Br

Family : Asclepiadaceae

**Vernacular Names:**

- *Sanskrit - Kshiraparna, Raktarka, Arkaparna, Arkanama, Vikirana, Shuklaphala,*
- *Marathi - Rui*
- *Hindi - Aak, Madar*
- *English - Madar*

**Rasa Panchaka**

**Rasa -** *Katu, Tikta*

**Virya -** *Ushna*

**Guna -** *Laghu, Ruksha, Tiksna*

**Vipak -** *Katu*

**Karma -** *Vatahara, Rechan, Dipana*

**Classical categorization**

**Charaka -** *Bhedaniya, Vamnopaga, Swedopaga*

**Sushruta -** *Arkadi, Adhobhagahara*

**Vagbhata -** *Arkadi*

**Types**

1) *Shwetarka - Calotropis* gigantea (Linn.) R. Br Ait.
2) *Raktaarka - Calotropis procera*(Ait.) R. Br

**Classification**

- Modern - Irritant, Organic, Vegetative poison.
- *Ayurveda - Sthavara, Akritrim, Vanaspatija Visha, Upavisha*

**Botanical Description**

*Calotropis procera* is an erect shrub that grows to a height of about 1-2 meters. Leaves are subsessile, broad, and oval, measuring 6-15 cm long and 4.5-8 cm wide. Flowers grow in umbellate cymes and are white, purple-spotted, or pink. Root bark taproots have prominent tips and a rounded head. Hard roots are grayish-white in hue. The bark is yellowish grey on the exterior and yellowish white inside. Root It is corky, squishy, and rough with longitudinal fissures.

**Parts used:** Root Bark, Flowers, Leaves, Roots, Latex (*Kshira*).

**Active Principles:** Calactin, Calotropin, Uscharin, β-amyrin, Calotoxins, Trypsin in *Kshira.*

***Karma* (Pharmacological action)**

***Ayurveda -*** *Vishaghna, Vedanasthapana, Deepana, Pachana, Swedajanana, Pittasaraka, Vamaka,*

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*Rasayana, Vranashodhana, Kushthaghna, Shothahara, Raktashodhaka Jantughna, Vamanopaga, Rechana, Krimighna, Amashayakshobhaka, Balya.*

**Modern -** Anticancer, Antiimplantation, Antimicrobial, Anticoagulant, Anthelmintic, Nematicidal, excessive fibrinolytic, Vermicidal, Spasmogenic, Stimulant, mild diuretic.

***Rogaghnata*** *- Udararoga, Gulma, Visha, Krimi, Kushtha, Arsha, Pleeha, Ajeerna, Vibandha, Vata, Yakrutvikara, Kandu, Agnimandya, Shotha, Vrana, Swasa, Kasa, Vishamajwara, Jeernajwara.*

***Arka Ksheera Shodhana***

To purify *Arka Ksheera, Tila* (*Sesamum indicum* Linn.) is fried and put into it. *Ela, Maricha, Nagahwa,* and *Pippali* are fried and added to *Arka Ksheera* in quantities of two or three.

**Formulations -** *Arka Lavana, Mahavishagarbha Taila, Abhaya Lavana, Dhanvantara Ghrita, Arkeshwar Rasa, Arka Kshara.*

**Fatal Dose:** uncertain

**Fatal period:** About 12 hrs.

Phytochemicals found in *Calotropis procera* have been documented in different portions of the plant; they are included in Table no. 1 part-wise.

**Table 1: Phytoconstituents of various parts of *Calotropis procera*.[10]**

| Parts used | Phytoconstituents |
|---|---|
| Root bark | Benzoylisolineolone, Benzoyllineolone, β- amyrin, Three oleanane type triterpenes namely calotropoleanyl ester, Proceroleanenol B and Proceroleanenol A. |
| Flower | Evanidin3-rhamnoglucoside and cyanidin 3-rhamnoglucoside Esters of β – calotropeols, β – amyrin, volatile and long chain fatty acids, esters of waxy acids, evanidin- 3- rhamnoglucosides and alcohols. |
| Latex | Voruscharin (0.45%), Calactin (0.15%), Calactin composed of calotropagenin and hexose, Uzarigenin, Syriogenin, Proceroside, Calotropin, Calactinic acid, Uscharin, ∝- amyrin, - β amyrin, - β sitosterol and calotoxin (0.15%) |
| Stem bark | β amyrin, a colourless wax, giganteol, small amount of tetracyclic terpene and traces of sterols |
| Leaves | β - amyrin, cardenolides, calotropin, calotropagenin. |

**Table 2: Main phytoconstituents of *Calotropis procera* and their biological activities[11]**

| Phytoconstituents | Biological activities |
|---|---|
| α amyrin | Anti-inflammatory, Anti-oxidant, Analgesic, Antitumor, Antiulcer, Cytotoxic, Gastroprotective, Hepatoprotective. |
| β amyrin | Anti-oxidant, Analgesic, Anti-inflammatory, Antiulcer, Gastroprotective, Hepatoprotective. |
| β sitosterol | Antioxidant, Anticancer, Antifertility, Antifeedant, Anti-inflammatory, Antihyperlipoproteinaemic, Antileukemic, Anorexic, Antibacterial, Antilymphomic, Antimutagenic, Antitumor, Antiviral, Antipyretic, Hepatoprotective, Hypoglycemic, Hypolipidemic, Ulcerogenic, Hepatoprotective, Hypoglycemic. |
| Stigmasterol | Antioxidant, Antinociceptive, Antiviral, Cancer-preventive, Hypocholesterolemic, Sedative. |
| Calotropin | Antitumor, Cardioactive, Proteolytic |
| Calactin | Cardioactive |
| Calotoxin | Cardioactive |

**Table 3: In Vitro Anticancer potential of Phytoconstituents of *Calotropis procera* by using MTT assay.[12]**

| SN | Phytoconstituents (class) | Plant part (extract) | Cell Line |
|---|---|---|---|
| 1. | Calactin (Cardinolides) | Latex (Chloroform) | MCF-7 |

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| | | | |
|---|---|---|---|
| 2. | Calotropagenin (Cardinolide) | Leaves (Chloroform and butanol fraction) | HepG-2 ,A-549<br>MCF-7<br>HCT-116 |
| 3. | Calotropin (Cardinilide) | Root bark (Methanol) | K562 |
| 4. | Calotroposides (H to N)<br>(Oxypregnanes) | Root bark (n-Butanol) | A549<br>U373<br>PC-3 |
| 5. | Calotroposides-S (Oxypregnanes) | Root bark (n-Butanol) | A549, U373<br>PC-3 |
| 6. | Frugosides (Cardinolides) | Root bark (Methanol) | A549<br>U373<br>PC-3 |
| 7. | Proceraside_A (Cardinolides) | Root bark (Methanol) | A549, U373<br>PC-3 |
| 8. | Ursane (Triterpene)<br>(Calotroprocerol A, Calotroproceryl acetate A,<br>Calotroprocerone A) | Root bark (Hexane fraction) | A549<br>U373<br>PC-3 |
| 9. | 5-Hydroxy-3,<br>7-dimethoxyflavone-4-O-B-glucopyranoside(Flavonoid) | Stem (Ethanol) | HT-29<br>HepG2<br>NIH-3T3 |
| 10. | 2”-Oxovoruscharin<br>(UNBS1244)<br>(Cardinolide) | Root bark (Methanol) | 58 human cell line |

## Various research studies of anti-cancerous activity of *Arka*

**Table 4: In Vivo and In Vitro anticancer activities of *Calotropis procera* w.s.r. to its different parts.**

| SN | Study Type | Activities | Parts/Extract used | Cell line used | Assessment | Outcome |
|---|---|---|---|---|---|---|
| 1. | In Vivo | Cytotoxic<br>Chemopreventive | Dried Latex (aqueous extract) | X-15<br>Transgenic mouse model | Hepatocellular carcinoma | Cytotoxic<br>Chemopreventive effect |
| 2. | In Vivo | Antitumor | Stem extracts-(Ethyl acetate, acetone and methanol extract) | Adult Swiss albino mice | Sarcoma<br>180 tumour | Antitumor<br>activity |
| 3. | In Vitro | Cytotoxic | Leaves extract | Human Hepatoma cell (HEPG2) | SRB Assay | Anticancer potential of Chloroform-methanol (9:1)elute |
| 4. | In Vitro | Cytotoxic | Leaves (methanol extract) | T47D Brest Cancer cell | MTT Assay | (Methanol fraction presence effective against cell T47D) |
| 5. | In Vitro | Cytotoxic | Stem Leaves (methanol extract) | HCT- 15 | Cytotoxic Assay | Cytotoxic |
| 6. | In Vitro | Antiproliferative | Root (methanol, hexen, aqueous, ethylacetate extract) | Hep 2 Cancer cell | MTT Assay | Antiproliferative<br>Activity |
| 7. | In Vitro | Anticancer | (methanol extract)<br>Leaves | MCF-7<br>Cancer cell line | MTT Assay | Anticancer<br>Activity |
| 8. | In Vitro | Cytotoxic | Root bark extract | CaCo2 & Neuro 2a | MTT & Neutral red assay | Cytotoxic |

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| | | | | | | |
|---|---|---|---|---|---|---|
| 9. | In Vitro | Antiproliferative | Root (alcoholic, hydro-aqueous and aqueous extract) | KB(Oral)<br>SNB-78 (CNS) | SRB Assay | Antiproliferative Activity |
| 10. | In Vitro | Cytotoxic | Stem- Hexane, Dichloromethane, Methanol, Ethyl acetate acetone | HL-60<br>CEM<br>HCT-8<br>B-16/F10 | MTT Assay | Cytotoxic |
| 11. | In Vitro | Cytotoxic | Whole plant alcoholic extract | A-549, Hep-2 (Liver)<br>502713,HT-29(colon)<br>IMR82 (Neuroblastoma) | SRB Assay | Cytotoxicity |
| 12. | In Vitro | Cytotoxic | Leaves, flowers, fruit ethanol extract | MCF-7<br>HCT 116<br>HepG-2<br>A 549 | Viability assay | Cytotoxicity |
| 13. | In Vitro | Cytotoxic | Methanol extract of flowers | Hep-2<br>Vero cell line | MTT Assay | Cytotoxicity shown |
| 14. | In Vitro | Anticancer | Leaves | Gr/Nt-G/Ln-18 | Cyto sensor | Anticancer Activity |
| 16. | In Vitro | Anti-tumor | Root bark protein | MCF-7<br>MDA-MB-231 | MTT-Assay<br>LDH Assay | Antitumor Activity |

## DISCUSSION

The daily count of cancer patients is rising. Therefore, the need today is to find new treatments. Many plants have been shown to have anti-cancer activity, *Calotropis procera* is one of them. *Calotropis procera* has anticancer, cytotoxic, antitumor, and antiproliferative activity in various cell lines and animal studies. After extensive literature research, many plant species of *Calotopis procera* contain many herbal compounds as shown in Table 1. These plants were studied for many biological activities such as anti-tumor activities, cytotoxic activities, anti-ulcer, antioxidants, etc. as shown in Table 2. The anti-cancer potential of plants using the MTT method on different cell lines. As shown in Table 3, the typical cell line is A-549.

Preclinical studies are discussed in table 4 , some of them are discussed as follow :-

1. In this study, the anticancer property of dry latex (DL) of *Calotropis procera* was evaluated in the X15-myc transgenic mouse model. The serum level of VEGF was significantly reduced in the treated mice compared to the control animals. Therefore, DL of calotropis *procera* shows anticancer activity in a transgenic mouse model.[5]
2. In this study, the in vivo antitumor activity of the stem extract was investigated in adult Swiss albino mice bearing 180 sarcoma tumors. The ethyl acetate extract and animals treated with acetone extract decreased tumor growth by 64.3 and 53.1%, respectively, with reversible toxicity to the liver and kidney.[4]

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3. In this study, the extract of *Calotropis procera* (Ait) R.Br. The leaves were tested against a human hepatoma cell line (HEPG2). The findings justify the usage of *Calotropis procera* (Ait) R.Br. The leaves are used as an anticancer agent in traditional medicine.[13]
4. In this study, the MTT test was used to investigate the anticancer activity of the methanolic extract of *Calotropis procera* leaves. The percentage of cell viability after 48 hours of incubation with total extraction was less than 30%, moreover, cell growth was significantly inhibited.[14]
5. In vitro test for cytotoxic activity of *Calotropis procera* stem and leaves methanol extract was performed on human cancer cell lines at concentration of 10, 30 and 100 µg/ml. The results showed the ability of cancer to the HCT-15 cell line (colon cancer) at different concentrations.[15]
6. The anti-tumor activity of *Calotropis procera* root extracts in methanol, hexen, aqueous, and ethylacetate was examined, along with a putative mode of action against Hep2 cancer cells. The findings suggest that *Calotropis procera* root extracts impede Hep2 cell proliferation through processes involving apoptosis and interruption of the cell cycle.[16]
7. In this study, the antibacterial and anticancer properties of a methanolic extract of *Calotropis procera* leaves were examined using the disc diffusion test and the MTT assay, respectively, against the MCF7 breast cancer cell line and methicillin-resistant Staphylococcus aureus (MRSA). The MCF7 cell line's growth is inhibited by the metabolic fraction of C. *procera* leaves, and the leaves' potential as an efficient antibacterial agent has also been demonstrated by the results.[17]
8. An aqueous extract of *Calotropis procera* (Ait.) R. Br. root barks was examined in vitro for cytotoxicity against the Neuro-2a and Caco-2 cell lines from the human intestine and mouse, respectively. The cytotoxic activity of these cell lines has been demonstrated by MTT and Neutral Red assays.[18]
9. Using human oral (KB) and CNS (SNB-78) cancer cell lines as a model system, this study examined the antiproliferative activity of three extracts—alcoholic, hydro-aqueous, and aqueous—as well as their fractions from the root portion of *Calotropis procera*. According to the results, C. *procera*'s roots are cytotoxic to human cancer cell lines in vitro, both oral and CNS.[3]
10. The MTT test was used in this study to evaluate the in vitro cytotoxic activity of five extracts from the stem of C. *procera*: ethyl acetate, acetone, hexane, dichloromethane, and methanol. Research indicates that stem extracts from ethyl acetate, acetone, and methanol exhibit encouraging antiproliferative properties in vitro on cancer cell lines.[4]

All these studies showed that different components of *Calotropis procera* have anticancer, antiproliferative, cytotoxic and antitumor activity. From the above information, it is clear that Caloropis *procera* leaf extract is used in cancer research. The MTT method and the SRB test are the most commonly used parameters. Since *Calotropis procera* is mostly used in research related to anticancer activities, the preparation of *Calotropis procera* may be useful as a cancer treatment.

## CONCLUSION

From the above review, extracts of different parts of *Calotropis procera* (*Upavisha Arka*) have shown potential anticancer activity in various in vitro and in vivo studies. The plant compounds of *Calotropis procera* were also tested as anticancer agents. Therefore, it can be concluded that *Calotropis procera* is highly carcinogenic among cancer types. This review may be useful in providing more information to conduct further clinical and clinical research on its use in the treatment of cancer and various diseases.

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