



Evaluation of Anticancer Activity in Amaranthaceae Members

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Abstract: Cancer, one of the dreadful diseases, is a rising burden for the worldwide. The people look for an alternative treatment solution to avoid the side effects that causing by chemical or radiation therapies. Herbal medicine provides a very feasible alternative to modern medicine against cancer. The herbal plants in Amaranthaceae play predominant roles in medicines against different types of human cancer by inhibiting the proliferation, metastasis and apoptosis of cell lines.

Keywords: Amaranthaceae, medicinal, anticancerous, cytotoxicity, ethnobotany

The dreadful disease, Cancer, severely affects the human population. The available medical treatments like chemotherapy can damage the health of the patient. From ancient time itself, the herbal medicines have been used as the source of medicines for various diseases. According to the World Health Organization (WHO), some nations still reply of plant based treatment as their main source of medicine and developing nations are utilizing the benefits of naturally sourced compounds for therapeutic purposes (Rao et al., 2002). Keeping this fact, an attempt has been made to analyze the work being carried out all over the world about the plants which are used as anticancerous agents. Since the naturally derived plant products are less toxic, scientists and researchers starts to pay more attention in this field now.

lites is the reason behind the medicinal properties of all the plants. Thus researchers have developed in to investigating the potential properties and uses of terrestrial plant extracts for the preparation of nanomaterial based drugs for diseases including cancer (Sivaraj et al., 2014). Many plant species are already being used to treat or prevent development of cancer. Multiple researchers have identified species of plants that have demonstrated anticancer properties with a lot of focus on those that have been used in herbal medicine in developing countries (Frieburghaus et al., 1996; Ochwang et al., 2014). Over 60% of anticancer agents have been derived from natural sources (Cragg & Newman, 2005). Amaranthaceae is such a family with lots of potential as medicine, and also many members are reported to have anticancer properties.

The presence of secondary metabo-

Amaranthaceae contains annual or

perennial, dioecious, monoecious or polygamous herbs, shrubs or rarely trees. It is composed of approximately 800 species of 60 genera with two sub families, Amaranthoideae with Gomphrenoideae (Iamonico, 2020). The family has a largely worldwide distribution and the members are common in deserts, estuarine or alkaline regions, tropical areas and some temperate regions (Simpson, 2010). The members of the family which are commonly used as a medicine for cancer treatment are *Achyranthes*, *Aerva*, *Amaranthus*, *Alternanthera*, *Celosia* and *Cyathula*.

1. Anticancer plants in Amaranthaceae

1.1. *Achyranthes* L.

Achyranthes is also known as 'Chaff Flower' which are mostly perennial or annual herbs. Stem is erect to ascending with opposite leaves. Inflorescences are terminal and axillary, pedunculate, elongate, many flowered, simple spikes or few branched panicles. Flowers crowded together at tips, becoming more widely spaced toward base. The bisexual flowers often become deflexed with age and bear 4 or 5 tepals. Utricles are indehiscent and one seeded (Robertson, 1981). The plants are distributed in Central and South-East United States, Mexico, West Indies, Central America, South America, tropical, subtropical and warm-temperate regions of the Old World.

The genus includes two famous medicinal species namely *A. bidentata* and *A. aspera*. *A. bidentata* which has used for the treatment of various diseases including amenorrhoea, dysmenorrhoea, lumbago, gonalgia, paraplegia, edema, stranguria, headache, dizziness, odontalgia, oral ulcer, hematemesis

and epistaxis (He et al., 2017). *A. aspera* is a well known medicinal plant used commonly in ayurvedic, Unani-Tibbi, Siddha, allopathic, homeopathic, naturopathic and home Remedies (Dhale & Bhoi, 2013). Different parts of the plant and the plant as a whole are used for medicinal purpose. The plant is bitter, pungent, heating, laxative, stomachic, carminative, and traditionally it is used to treat fever, dysentery, diabetes, vomiting, bronchitis, heart disease, piles, itching, abdominal pains, ascites, dyspepsia, blood diseases, tooth ache, gonorrhoea, cough and stomachic and digestive problems (Girach et al., 1992; Chopra, 1933; Rangari, 2006; Dwivedi et al., 2007). The addition of *A. aspera* would enhance the efficacy of any drug of plant origin and can be used as a supporting agent (Hasan, 2014).

Anticancer activities: *A. aspera* suppresses the cell proliferation and increases cytotoxicity in colon cancer cells. This ability could be attributed to the induction of apoptosis via the mitochondria mediated pathway and arresting the cells in S phase of cell cycle in COLO-205 cells. They could promote the release of cytochrome c by regulating Bcl-2 family proteins and activate caspase-9/-3 to trigger cell apoptosis, decrease Akt-1 transcription (Subbarayan et al., 2012; Arora & Tandon, 2014; Omidiani et al., 2020). The extract from *A. aspera* has cytotoxic effects against VERO (monkey healthy kidney epithelial) cells, AGS (human stomach cancer cells), MCF-7 (human breast cancer cell line), A549 (human lung cancer cells) and COLO 320 DM (human colon cancer cell line) (Baskar et al., 2012). The leaves of *A. aspera* contain anti-proliferative compounds with specific activity against

pancreatic cancer (Subbarayan et al., 2012). At the same time, in Dalton's Lymphoma (DL) cells treated with methanolic extract, the protein kinase C α (PKC α) pathway inhibits in a concentration-dependent manner. (Singh et al., 2021). *A. aspera* roots extract in acetone has the maximum cytotoxicity against HeLa, colon and liver cancer cell lines (Singh et al., 2017; Omidiani et al., 2020).

1.2. *Aerva* Forssk.

Aerva species are perennial herbs with salient morphological characters. They constitute prostrate to erect stem, alternate branches and leaves with entire margins, hermaphrodite flowers, oval or oblong perianth and membranous and margined sepals. Flowers usually bear five stamens which are shortly monadelphous at the base. The single pendulous ovule containing ovary possesses slender and distinct short style. Two stigmas are present which are short to long and thread like. The seeds are compressed which are reniform, firm and black (Alwadie, 2005). There are approximately 28 species of *Aerva* species, but only a few are medicinal of which *A. persica*, *A. lanata* and *A. javanica* exhibit great medicinal values. A number of flavonol glycosides including aervanone, kaempferol-3-galactoside and isorhamnetin-3-O- β -D-glucoside, are the major phytoconstituents in *A. persica* and the minor constituents include β -cyanins (glycine betaine and trigonelline), sterols and carbohydrates (Chawla et al., 2012). *A. lanata* is an important medicinal plant widely used in traditional systems of medicine like ayurveda and Siddha. It belongs to the Pashanbheda group of plants used to cure urinary stones. The plant possesses a wide

variety of healing applications in traditional and folklore medicines of various geographical locations. It comprises of an extensive range of phytochemicals such as canthin-6-one, β -carboline alkaloids, flavonoids, phenolic acids, steroids and terpenoids. Due to the presence of the phytocompounds, the plant bears anti-urolithiatic, diuretic, hepatoprotective, anticancer, immunomodulatory, antioxidant, antimicrobial and numerous other pharmacological activities (Mandal & Madan, 2016).

Anticancer activities: Ethanolic extract of whole plant of *A. lanata* exhibits immunomodulatory and antitumour activity. It enhances the total WBC count, bone marrow cellularity and number of α -esterase-positive cells (Siveen & Kuttan, 2012; Kumar et al., 2013). Treatment also shows enhanced proliferation of splenocytes, thymocytes and bone marrow cells both in the presence and absence of specific mitogens in vitro and in vivo. Both aqueous and ethanolic extracts decrease the average increase in body weight, reduce the packed cell volume and viable tumour cell count and increase the life span of Dalton's Ascitic Lymphoma (DAL) treated mice in turn brought back the haematological parameters, serum enzyme and lipid profile near to normal values (Rajesh et al., 2011).

1.3. *Alternanthera* Forssk.

The members of the genus are annual or perennial herb with prostrate or ascending stems and simple leaves. Inflorescence is axillary and terminal, sessile or peduncled, many flowered cylindrical spikes or spheric heads with persistent bracts and bract lets. Flowers are bisexual, white, glabrous or woolly with 3-5 stamens fused at base into short tube and 5

pseudo staminodes alternate with stamens. The plants have an ovoid to spheric ovary with short style and stigma. Fruits are indehiscent with one seed. The genus comprises about 170 species worldwide and generally distributed in tropical America (Iamonico & Pino, 2016).

Anticancer activities: Some members of *Alternanthera* are widely used in the treatment of cancer. The cytotoxicity of *A. sessilis* plant parts induces anticlonogenic property on the HT 29 cancer cells and causes cell growth inhibition and activation of apoptosis (Hanahan et al., 2014). The plant parts act in a dosage dependent manner and the ethanolic leaf extracts become active for the treatment of colon cancer (Gothai et al., 2018). Similar to this, the ethyl acetate extract of *A. brasiliensis* shows significant decrease in tumour volume, viable cell count, tumour weight and life span of EAC tumour bearing mice in a dose dependent manner (samudrala, 2015). At the same time, the hematological profile count of RBC, hemoglobin and WBC revert to normal level. The cytotoxic, antiproliferative and antimigratory properties of ethanol based extracts of the aerial portions of *A. bettzickiana* inhibit the cell growth and proliferation of breast (MCF-7), liver (HepG2) and cervical (HeLa) cancer cells (Saengha et al., 2022).

1.4. *Amaranthus* L.

The plants are typically annuals or short lived herbs. The stem of monoecious or dioecious is armed with spines and bears simple alternately arranged leaves. The small flowers arranged in dense showy inflorescences. A single plant can produce hundreds or thousands of seeds, borne singly in dry capsule fruits. The plants utilize a photosynthetic

pathway known as C4 carbon fixation, which largely prevents photorespiration and thus increases drought tolerance. Several species of *Amaranth* utilize for food as well as medicines by native tribal people in many countries.

Anticancer activities: Methanolic extracts of *Amaranthus spinosus* have the ability to inhibit cell proliferation and induce apoptosis in cancers of breast (MCF-7), colorectal (HT-29), liver (HEP-G2) and normal cell lines (Rajashekar et al., 2014). The upregulation of p53, Bax and caspase-3 and downregulation of Bcl-2 mRNA in *Amaranthus* treated mice indicates the mitochondria mediated apoptosis of EAC cells (Al-Mamun, 2016). The ethyl acetate extracts of *A. viridis* and *A. spinosus* show greater anticancer activities against HT-29 and Hep G2 cancer cells (Jin et al., 2013).

1.5. *Cyathula* Blume

The species under *Cyathula* are prickly chaff flowering plant. It is a small sized weed, reaching height up to 10-20 cm height. Stems are violetish red in colour and the leaves are simple, opposite, exstipulate, short petioled, rhomboid or ovate (Vijayakumar et al., 2014).

Anticancer activities: Of the members of the genus, *C. prostrata* has high potential as an anticancer drug. Methanolic extract of *C. prostrata* leaves has antitumour activity which reduces the tumour growth, viability of tumour cells and raising life span by preventing the lipid peroxidation in turn promoting the antioxidant systems in Dalton's lymphoma ascites induced mice (Priya et al., 2013). The extract of *C. prostrata* induces apoptosis via the extrinsic pathway, and this activation is

independent of the mitochondria. The extract acts through multiple targets by inducing cell cycle arrest in the G1 phase through an unknown mechanism, apoptosis through an extrinsic death receptor pathway and replicative senescence through inhibition of telomerase (Schnablegger, 2010).

1.6. *Celosia* L.

Celosia species are annual or perennial herbs, edible and ornamental plants, consisting of about 60 species worldwide, is native to subtropical and temperate zones of Africa, South America, and South East Asia. The flowers are edible and ornamental. The generic name is derived from the Greek word kelos, meaning "burned," and refers to the flame like flower heads. If the flower heads are crested by fasciation; it is called as 'Velvet flower' (Thorat, 2018)

Anticancer activities: *C. argentea* consists of 2 important phytoconstituents; a flavonoid, luteolin-7-O-glucoside (Compound 1), and a

phenolic compound, 1-(4-hydroxy-2-methoxy-benzofuran-5-yl)-3-phenylpropane-1,3-dione (Compound 2). Presence of benzopyran and hydroxyl groups in compound 1 and benzofuran, dione, and hydroxyl groups in compound 2 serve a basis for their anticancer potential (Rub et al., 2016).

2. Outlook

Anticancer agents discovered from medicinal plants have played a major role in cancer treatment. It is documented that medicinal herbs have rich anticancer potential due to their immunomodulatory and antioxidant properties. Many studies have reported inhibition of enzymes that stops tumour growth. Studies are needed to highlight the mechanism of anticancer action of many already explored and many unexplored plants. Among the family Amaranthaceae, the members of the genera *Achyranthes*, *Aerva*, *Alternanthera*, *Amaranthus* and *Cyathula* are widely using for the treatment.

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