



# The Genus *Inula* (Asteraceae) as Source of Anticancer Agents

Gouthami V.

PG Department of Botany, Korambayil Ahamed Haji Memorial Unity Women's College  
Manjeri, Malappuram, 676122, Kerala, India.

Corresponding author: gouthamimanjeri@gmail.com

**Abstract:** Cancer is a group of more than 100 distinct diseases characterized by the uncontrolled growth of abnormal cells in the body. The World Health Organization has estimated that the global cancer burden could be reduced by as much as 30 to 50% through prevention strategies, particularly through the avoidance of known risk factors. Medicinal plants have a role in curing and avoiding such cell proliferation. The local people used the plants in a traditional way for all health problems from the ancient period. One of the plant genera, *Inula*, belongs to the tribe Inuleae and the family Asteraceae with about 100 species. Diverse biological activities have been attributed to this genus including anticancer, antibacterial, hepatoprotective, cytotoxic and antiinflammatory. The species growing in East Asia are widely used by the local people for varied medicinal properties which have prompted many workers to study the phytochemistry of these species that ultimately resulted in the extraction of a number of novel bioactive molecules. This emphasizes the need for extensive study for revealing the medicinal importance of the other species of *Inula*.

**Keywords:** *Inula*, anticancer agents, secondary metabolites, antiproliferative, Asteraceae

Over a decade the number of cancer patients is increasing in the world. The research field always seeks new medicines and treatments for different cancer. Plants take place a vital role in the manufacturing of medicines because plants produce lots of secondary metabolites that are beneficial to major biological activities of organisms. Moreover, 80% of the population depends on traditional medicinal plants. We have a glorious history of traditional medicines. Our cultural legacies like the Vedas and Upanishads show the plethora of wisdom on the plant kingdom. The largest group of the plant kingdom is

angiosperms, in which the Asteraceae family is one of the larger families.

Asteraceae is commonly known as the sunflower family and is under the Asterales order. The family included 1600 genera and 2500 species. Many species are used for diet and medicinal purposes. Most species are great sources of inulin, a natural polysaccharide with solid prebiotic properties. It has potent antioxidant, antiinflammatory, antimicrobial activity, anticancer, diuretic and wound healing properties. All species of the family have phytochemical compounds including polyphenols, phenolic acids, flavonoids, acetylene and

terpenoids. The genus *Inula* contains more than one hundred species in temperate region of Europe and Asia. The genus first described by Linnaeus in 'Species Plantarum' (1753). In India total 17 species and two varieties are represented (Karthikeyan et al., 2009). The genus comprises annual or perennial herbs in India. Characters of the genus is flowering heads (capitula), which are heterogamous and with both ray and disc florets. The capitula are usually arranged in terminal corymbs or cymes but in some taxa, they are solitary and pedunculate or sessile and densely congested at the center of the rosulate leaves. *Inula* members have some ethnomedicinal uses, while some members face habitat loss. Hence, some species are endemic including *I. racemosa* and *I. rhizocephala* (Rao & Datt, 1996).

## 1. Anticancer species in the genus *Inula*

### 1.1. *Inula viscosa* (L.) Aiton

This is a highly branching perennial plant common throughout the Mediterranean Basin. It has long, narrow leaves that are pointed at both ends and have teeth along the edges and glandular hairs on the surfaces. One plant can produce many yellow flower heads each with as many as 16 ray florets and 44 disc florets.

**Anticancer activities:** It is a generally used folk medicine with antiinflammatory and antiseptic activities. The plant contains twenty one components; among them, patchulane, 3-ethyl-3hydroxy-5alpha-androstan-17-one and  $\gamma$ -gurjunene are prominent. The species shows high antioxidant capacity, high rate of secondary metabolites and demonstrated neu-

roprotective activities (Qneibi et al., 2021). Tomentosin is considered a traditional remedy for the treatment of different types of cancers, which is present in the species. Traditionally, the plant is used for lung cancer.

### 1.2. *Inula helenium* Hook.f. & Thomson

The plant is a rhizomatous, sunflower like composite of the aster family that is native to Europe and northern Asia, but has naturalized in fields, clearings, disturbed sites, roadsides, and waste places in parts of eastern North America from Nova Scotia to Minnesota, South to North Carolina and Missouri. It typically grows to 3-6' tall. It is noted for having coarse, toothed, rough hairy leaves. Ovate-elliptic basal leaves typically grow to 1-2' long on petioles extending to as much as 1' long. Ovate-lanceolate stem leaves are much shorter and sessile, decreasing in size from the bottom to the top of the central rigid hairy stalk. Sunflower like flowers (2-3" diameter) subtended by broad floral bracts, feature numerous very thin, scraggly yellow rays which surround a central disk of darker yellow tubular flowers. Flowers bloom July-September.

**Anticancer activities:** The plant has a long and interesting history as a medicinal herb wherein the rhizomes and roots are at one point, using in a large variety of medical applications primarily in the treatment of respiratory type ailments. The plant widely used in folk medicine to treat many diseases including bronchitis, cough, lung disorder, tuberculosis, intestinal ulcers etc. The major component of the plant extract is sesquiterpene lactones and eudesmanolides, exhibiting diverse bioactivities such as antitumour, antiinflammatory, antimicrobial, antiproliferative and antibacterial

(Konishi et al., 2002). The plant is an efficient inhibitor of the human U87 MG glioma cells. Therefore, the aerial parts are a valuable source for the development of a new chemotherapeutic drug for brain cancer.

### 1.3. *Inula britannica* L

The common names of the plant are 'British Elecampane', 'British Yellowhead' or 'Meadow Fleabane'. It is an erect, rhizomatous, sunflower like, herbaceous biennial or perennial in the composite family. Once established in the landscape, the plant will spread aggressively and rapidly by seeds, rhizomes or root fragments.

**Anticancer activities:** Flowers of the plant are used as traditional Chinese and Kampo Medicines which are rich source of secondary metabolites. These consist of terpenoids like sesquiterpene lactones and dimmers, diterpenes, triterpenoids and flavonoids. The isolated compounds have shown diverse biological activities like anticancer, antioxidant, antiinflammatory, neuroprotective and hepatoprotective. The sesquiterpenoids, OABL and OODABL isolated from the species induce phosphorylation of BCL-2 in breast, ovary and prostate cancer cell lines.

### 1.4. *Inula falconeri* Hook.

The plant is annual herbaceous that vary greatly in size from small species of few centimeters tall. They carry yellow daisy like composite flower heads often with narrow ray florets.

**Anticancer activities:** Alantolactone and sesquiterpene lactone help cytotoxic activity against solid tumours and several acute myeloid leukemia stem cell lines.

### 1.5. *Inula royleana* DC.

Kashmir *Inula* is found in the Himalayas, from Pakistan to Kashmir, at altitudes of 2100-4000 m. It is common and prominent in Kashmir. The plant is stout erect with very large handsome golden-yellow flower heads of 10-12.5 cm across, much larger than those of showy *Inula*. Ray florets are numerous, up to 5 cm long. Leaves are large, elliptic-lance shaped. Lower leaves are elliptic-blunt, 15-25 cm, with an equally long winged leaf stalk. Upper stem leaves are elliptic, up to 20 cm, with enlarged stem clasping base. The stem is unbranched 1-2 feet tall. Flowering period is July-September.

**Anticancer activities:** The plant is an ethno medicine, used as antiinflammatory and antitumour agent due to the presence of diterpene alkaloids, alantolactone and sesquiterpene lactone. The plant shows antiproliferative activity against different cancer cell lines of lung cancer (Stojakowska & Malarz, 2004).

### 1.6. *Inula racemosa* Hook.

The plant is a critically endangered Himalayan herb. The species is a perennial herb up to 1.5 m tall with fragrant prominent root and root stock. Stems are many in number, ascending from the base of the rootstock. Leaves are leathery, rough above and densely hairy below, 25-50 cm long, 10-12 cm broad and elliptic-lanceolate in shape.

**Anticancer activities:** Alantolactone, sesquiterpene lactone,  $\beta$ -sitosterol, isoalantolactone, dihydroalantolactone and other secondary metabolites are present in leaf and root of the plant. Anticancer activity detected in this plant but further research is not investigated. Normally, the plant is using by the ethnic comm-

unities for breathlessness, asthma and lung cancer.

### 1.7. *Inula rhizocephala* var. *rhizocephaloids* (Clarke) Kitam

The species is endemic to Nubra and adjacent ranges of Ladakh. It is a stemless species and easily distinguished by its rosette of leaves flat on the ground and a domed stalkless cluster of yellow flower heads at its center. Flower heads are 1.9-2.5 cm across, ray florets yellow, about 8 mm, involucre bracts linear pointed, outer ones green with curled tips, inner ones purplish. Leaves are pressed to the ground, long spoon shaped, blunt, narrowed into a broad stalk, bristly haired, usually 3-5 cm long. The plant is usually 7-12 cm across. Fruits are brown, round, longitudinally finely ribbed, covered with appressed short fox-red hairs or hairless. Pappus is as long as achene, with numerous bristles. Flowering period is June-August.

**Anticancer activities:** It is ethnomedicine used for treating colds, cough, chest complaints and lung cancer. Alantolactone and sesquiterpene lactone are extracted from the plant which induce the medicinal properties. It can be used as anticancer drugs in future, if the research proved the cancer inhibition potentials of the plant extracts.

### 1.8. *Inula grantioides* Boiss

The plant is a perennial herb, up to 50 cm high, moderately branched. Cortex is green, striped, glandular-hairy. Leaves are linear to spoon shaped, entire to 3 lobed at tip, flattened, fleshy, 6 x 2 cm, gradually narrowing towards the base, glandular-hairy. Flower heads are more or less solitary, radiate with

herbaceous bracts externally. Involucre is cup shaped, involucre bracts about 70 in several rows, linear to oblong, pointed, dorsally glandular, spreading at anthesis. Ray florets are 5-13, 9-20 x 2-5 mm, blade oblong to almost linear, apically 2-3 finely toothed. Disc florets are 40-90; flower 6-11 x 1.5-2 mm, style about 7 mm long. Flowering period is November-May.

**Anticancer activities:** A new flavonol, grantioidin, has been isolated from *Inula grantioides* and its structure determined as 5-hydroxy-3,6,7,2',5'-pentamethoxyflavone.  $\beta$ -Sitosterol, lupeol, taraxasterol, taraxasterol acetate and tricontanol also isolated for the first time from this plant. This plant is used for pancreatic cancer treatment (Ahmad & Ismail, 1991).

### 1.9. *Inula helianthus-aquatica* C. Y. Wu

The plant is herbaceous perennials or subshrubs, mostly with large basal leaves and daisy like yellow flower heads, often with narrow ray florets. Many of the species are popular for the garden, with cultivation going back to antiquity. The smaller species are used in rock gardens and the more common larger ones, which tend to have very coarse foliage in borders. The plant includes different secondary metabolites having medicinal activities like alkaloids, flavonoids, saponins, terpenoids, steroids, glycosides etc.; hence the plant shows antioxidant, antitumour, antibacterial, antiviral, antidiabetic and antiinflammatory properties. It makes the species highly medicinal in pharmacology.

**Anticancer activities:** Seven compounds were isolated and elucidated from the plant namely inuchinenolide B, 8-epi-florilenalin-2-O-acetate,

neogaillardin, tomentosin, atractyligenin,  $\beta$ -sitosterol and  $\beta$ -hydroxypropiovanillone. from the plant. All the compounds are isolated from the flower of *Inula helianthus-aquatica* for the first time which is used against lungs, stomach, intestines, uterine neck, nasopharynx and bladder cancer cells.

## 2. Outlook

Asteraceae is one of the largest families of flowering plants with key character of head inflorescence. The plants bear numerous

trichomes which also exhibit the characteristic flavour due to the presence of secondary metabolites that are not essential for the primary growth and development of the plant. But they possess different biological activities such as antioxidant, antidiabetic, antitumour, antimicrobial etc. due to the presence of these compounds. Hence, the family members may contribute more in the field of medicinal industry in future, especially in cancer prevention and controlling drug designing areas.

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