

## Anticancer Properties of Datura Genus

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### ABSTRACT:

One of the most dreadful illnesses that plagues people worldwide on a constant basis is cancer. Cancer is a condition in which some body cells begin to grow quickly and uncontrolled, with the potential to spread to other body regions. Nearly every part of the body might become cancerous. This is due to the fact that genetic mutation of the cells or activation of the onco gene, which is present in all cells, is the primary cause of cancer cells to arise. The start of the disease has been mostly attributed to the inactivation of tumour suppressor genes, chromosomal rearrangements, chemical carcinogens, impulsive changes, and viruses. Depending on where they start, cancers can be classified as leukaemia, bone cancer, breast cancer, prostate cancer, etc.

One of the biggest causes of mortality worldwide is cancer. Additionally, it is among the world's major causes of death. In its advanced stages, cancer is nearly incurable.

Various research works conducted have shown results which are favourable in helping to conclude that Datura plants has Anti-cancer properties in them. Tests conducted on different cells have shown positive results on plant's anticancer properties. Identification of different chemical compounds having anticancer properties have helped in research for the treatment of cancer.

### KEYWORDS:

Datura, cancer, Solanaceae, Withanolides, Isowithametelin

### I. INTRODUCTION:

Everywhere in the globe, there are cases of cancer. In 2020, there were 10.3 million new cases of cancer (excluding nonmelanoma skin cancer), 18.1 million cancer deaths (including nonmelanoma skin cancer), and 19.3 million new cancer cases. Prostate cancer, which is also the second most prevalent cause of cancer-related deaths in men, is more frequently diagnosed than breast cancer in women.

The most prevalent type of cancer in women worldwide is female breast cancer (11.7%), followed by lung (11.4%), colorectal (10%), prostate (7.3%), and stomach (7.3%) (5.6 percent). Lung cancer accounts for 18% of all cancer-related fatalities, followed by colorectal (9.4%), liver (8.3%), stomach (7.7%), and female breast cancer (6.9 percent). The number of cancer cases worldwide is predicted to increase by 47 percent from 2020 to 28.4 million cases in 2040 due to demographic changes, with a greater increase in developing (64 percent to 95 percent) than developed (32 percent to 56 percent) countries. However, this may be made worse by rising risk factors brought on by globalisation and an expanding economy. Leukemia is a malignancy that often develops in the bone marrow but soon spreads to the blood. Leukemia's precise origin is still a mystery. There might be a role for viral, genetic, environmental, or immunological causes.

More than 60% of the currently utilised anticancer drugs have their origins in these same natural resources, which include at least 3000 plants that have anticancer effects.[2] The Solanaceae family plant genus Datura is one of those with anticancer characteristics. The genus is known by several different common names, including Jimson weed, Downy datura, and Thorn apple. Alkaloids of many different types, including hyoscyne, hyoscyamine, fastusine, littorine, acetoxytropine, and valtropine, are abundant in the plant species. Additionally, it contains calystigines with glycosidase inhibitory activities and different withanolides with anticancer characteristics.[3]

The Datura genus, usually referred to as Jimson weed or Datura, is a member of the Solanaceae family. Numerous applications for its seeds include purgative, cough, fever, and asthma treatment. The alkaloids atropine and scopolamine are the main physiologically active components of datura. The datura plant has both therapeutic and toxic effects. Studies have also demonstrated that it has excellent pharmacological potential and high utility. Datura seeds are used as analgesics, antihelmintics, and

anti-inflammatory medications to treat infestation, gastrointestinal discomfort, toothaches, and fever from inflammation.[4]

## PHYSICO-CHEMICAL CHARACTERISTICS:

### Physical characteristics:

Nine species of *Datura*, including *Datura ceratocaula*, *Datura discolor*, *Datura ferox*, *Datura innoxia*, *Datura leichhardtii*, *Datura metel*, *Datura quercifolia*, *Datura stramonium*, and *Datura wrightii*, make up the genus in the Solanaceae family. Due to its role in an unintentional poisoning that occurred at Jamestown, Virginia, it became known as Jimson weed or Jamestown weed. Other frequent names for *Datura* include deadly nightshade, belladonna, metel nut, thorn apple, devil's apple, and devil's trumpet.

The term "datura" refers to a species of herbaceous shrubs. It is a pubescent plant with branches that ranges in height from 60 to 120 cm. Lobed alternate leaves about 10 to 20 cm long and 5 to 18 cm broad make up this plant. The tall, white to pale purple, trumpet-shaped blooms are another distinctive characteristic. They range in length from 5 to 20 cm. The fruit of the datura plant measures 4 to 10 cm in length and 2 to 6 cm in width. A large number of kidney-shaped seeds are released as the fruit breaks open, covering fields, pastures, and wastelands (Figure). *Datura* and the genus *Brugmansia* have structural similarities. *Brugmansia*, a species of woody shrub that was originally grouped with *Datura*, is recognised by its pendulous blooms and lack of spines on the fruit capsule.

### Chemical characteristics:

Scopolamine, hyoscyamine, and atropine, the tropane alkaloids found in the plant, are mostly concentrated in the seeds and flowers. These alkaloids competitively inhibit the parasympathetic nervous system end organ sites as well as central and peripheral muscarinic receptor sites for the neurotransmitter acetylcholine. Scopolamine causes central nervous system side effects such as delirium, agitation, sleepiness, and dementia by crossing the blood-brain barrier. Although *Datura* has been shown to possess therapeutic qualities such as antinociceptive, antioxidant, anti-inflammatory, antibacterial, anti-asthmatic, anti-rheumatoid, and hypoglycemic capabilities, its medical application has not yet been proven. For its antispasmodic effects on the gastrointestinal, biliary, and genitourinary systems as well as for use as a pre-anesthetic drug, scopolamine is available

as butyl bromide. During medical-legal investigations, scopolamine is also employed as a truth serum.[5]

## II. RESULT AND DISCUSSION:

In the initial study, the different concentrations of the compound isolated from the ethyl acetate fraction of *Datura stramonium* flowers were subjected to the MTT assay, with the results displayed in the table [Table 1]. The CTC50 values for the human liver cancer HePG2 cell line are shown to be 79.43 g/ml, 64.15 g/ml, 58.63 g/ml, 49.52 g/ml, and 37.48 g/ml for the sample concentrations of 1000 g/ml, 500 g/ml, 250 g/ml, 125 g/ml, and 62.5 g/ml, respectively.[Table 1][6]

The *Datura stramonium* flower component, which was isolated from the ethyl acetate fraction, has anticancer activity at all concentrations, according to the MTT experiment. This study contributes to the conclusion that *Datura stramonium* has anticancer properties.[6]

In a different study by Fatima et al. (Fatima et al., 2020), scientists isolated the withanolide, isowithametelin, a cytotoxic and cancer-chemopreventive withanolide, from the leaves of *D. innoxia*. By gradually raising the system's polarity, the EtOAc-MeOH crude extract was fractionated on a SPE column with hexane, hexane-EtOAc, EtOAc, EtOAc-MeOH, and MeOH. Then, using single crystal X-ray diffraction as previously described by Sinha et al., a molecule that had been separated using chromatographic techniques such normal-phase MPLC and VLC was identified as a withanolide (isowithametelin) (1989). The Cambridge Crystallographic Data Centre (CCDC) has received the crystallographic data under number 1912175. White crystals in the form of needles were used to isolate isowithametelin.[7]

Withanolides have a variety of pharmacological actions, including anti-inflammatory, immunosuppressive, antioxidant, and anticancer effects. Withanolides have the ability to initiate the phase II enzyme quinone reductase, halt angiogenesis and tumour cell growth (Haq et al. 2013). Using the SRB test and MTT-based in vitro cytotoxicity assays, the compound's cytotoxic efficacy against cancer cell lines was evaluated [Table 2]. With IC50 values of 4.3 0.93, 6.9 1.3, and 0.01 0.001 g/ml for MCF-7, LU-1, and PC-3 cell lines, respectively, isowithametelin shown significant cytotoxicity. The remarkable IC50 values for 1 are well matched to those for doxorubicin (positive control) against

various cell lines, i.e., MCF-7 (3.2 0.15 g/ml), LU-1 (4.5 0.20 g/ml), and PC-3 (2.95 0.98 g/ml), indicating significant potential. The high prevalence of these tumours and the necessity to create effective chemotherapeutic drugs led to the selection of the cell lines for this investigation. For instance, prostate cancer is the most typical form of cancer in males, but breast cancer is the most typical form of cancer in women. Additionally, lung cancer accounted for 18.2% (1.7 million fatalities) of all cancer-related deaths globally in 2015, making it the most prevalent kind of cancer (Segun et al. 2019). The ability of the isolated withanolide to prevent cancer was evaluated in this study using two assays, namely the inhibition of TNF-activated nuclear factor-kappa B (NF-B) and the inhibition of nitric oxide (NO) production in lipopolysaccharide (LPS)-activated murine macrophage RAW 264.7 cells (iNOs).[7]

Recent research has revealed that NF-B is a crucial transcription factor that regulates the expression of genes associated to cell survival, differentiation, inflammation, and adhesion growth, and is consequently implicated in carcinogenesis (Orlowski and Baldwin 2002). The substance showed no discernible inhibitory action in the TNF-activated NF-B test (Table 2). N-tosyl-L-phenylalanine chloromethyl ketone (TPCK), a positive control in this experiment (IC<sub>50</sub> = 10.8 1.7 g/ml), was employed. However, when tested for its ability to prevent NO production, isowithametelin [Figure 1] showed a strong inhibitory potential of 66 3.4% and an IC<sub>50</sub> value of 18.5 1.8 g/ml [Table 3]. The assay's positive control, NG-monomethyl-L-arginine (L-NMMA) (IC<sub>50</sub> = 25.1 2.3 g/ml), was employed. Table 3 displays the chemical 1's ability to inhibit protein kinases in action. In this test, an isowithametelin-loaded disc had an inhibitory zone

that measured 7 mm by 0.52 mm in clearness and 10 mm by 2.76 mm in baldness (MIC: 20 g/disc). The lack of a growth inhibition zone in the case of DMSO (the negative control), in contrast to surfactin (the positive control), which created a 27-mm bald growth inhibition zone, demonstrated the non-toxic nature of the substance.[7]

The study came to the conclusion that additional research to evaluate *in vivo* efficacy would be worthwhile given the significant cytotoxic activity of isowithametelin against the tested cell lines and its potential to treat cancer based on the NO inhibition testing.[7]

### III. CONCLUSION:

Plants have long been utilised for food, tanning, gum, oil, shelter, fibre, latex, and other things. Because they are a plentiful supply of vitamins, minerals, proteins, antioxidants, and carbs, plants also have an immuno-modulatory impact. We deduced from the facts provided above that the *Datura* genus, with its therapeutic characteristics, can be used to treat cancer.[8]

It was discovered that the *Datura* extract has immunostimulating properties that increased cell proliferation, cell surface indicators, cytokine production, and the cytolytic capacity of peripheral blood lymphocytes. Additionally, substances in *Datura* extract enhanced immune cells' ability to cause ROS production and mitochondrial depolarization to cause target cells to undergo apoptosis. In conclusion, chemicals found in *Datura* extract may be investigated as a possible new source of natural anti-inflammatory, immunomodulatory, and antioxidant agents for the treatment of cancer.[9]

#### TABLES:

Sr. No.	Concentration (µg/ml)	%CTC50 Cytotoxicity (µg/ml)	CTC50
1	1000	79.43	
2	500	64.15	
3	250	58.63	131.53
4	125	49.52	
5	62.5	37.48	

**Table 1:** The CTC50 values of the compound isolated from the ethyl acetate fraction of *Datura stramonium* flowers against human Liver cancer HePG2 Cell line

	MCF - 7		LU - 1		PC - 3	
	%Survival at 20 µg/ml	IC50 ( µg/ml)	%Survival at 20 µg/ml	IC50 ( µg/ml)	%Survival at 20 µg/ml	IC50 ( µg/ml)
Isowithametelin	10.5 +/- 16.2	4.3+/-0.93	24.35+/- 0.53	6.9 +/- 1.30	7.34 +/- 2.87	0.01 +/- 0.001
Doxorubicin	2.5 +/- 5.6	3.2+/- 4.76	5.67 +/- 4.76	4.5 +/- 0.20	4.65 +/- 2.34	2.95 +/- 0.98

Values (mean ± SD) are the average of three samples, analyzed individually in triplicate (n = 3). IC50, sample concentration which caused 50% inhibition of cell growth.

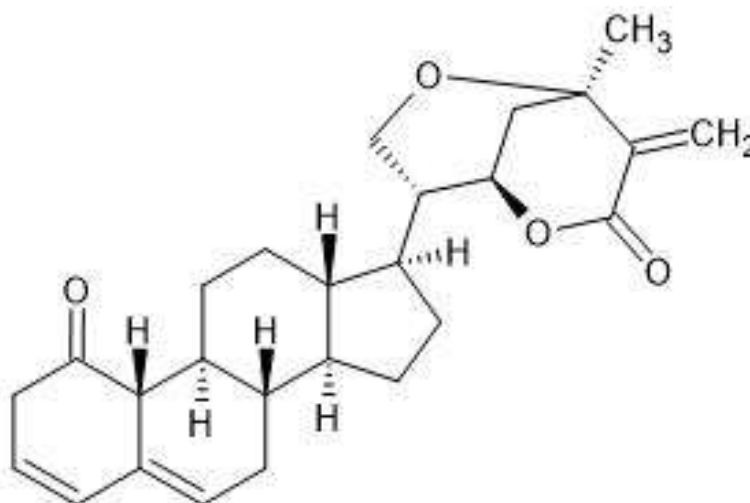
**Table 2:** Cytotoxicity assessment of isowithametelin isolated from *Datura innoxia* against MCF-7, LU-1, and PC-3 cell lines

Cancer chemopreventive assays	TNF-α-activated NF-κB inhibition			Inhibition of NO production		
	% inhibition (20 µg/ml)	% survival (20 µg/ml)	IC50 ( µg/ml)	% inhibition (20 µg/ml)	% survival (20 µg/ml)	IC50 ( µg/ml)
Isowithametelin	50.00 +/- 7.1	50.00 +/- 8.60	>20	66 +/- 3.4	78.3 +/- 5.2	18.5 +/- 1.8
TPCK			10.8 +/- 1.7			**
L-NMMA			**			25.1 +/- 2.3

Values (mean ± SD) are the average of three samples, analyzed individually in triplicate (n = 3). Cytotoxicity determination was performed simultaneously to avoid false positive results. IC50, 50% inhibitory concentration; TPCK, Nα-tosyl-L-phenylalanine chloromethyl ketone was used as a positive control in TNF-α-activated NF-κB inhibition assay; L-NMMA, NG -monomethyl-L-arginine was used as a positive control in the NO assay.

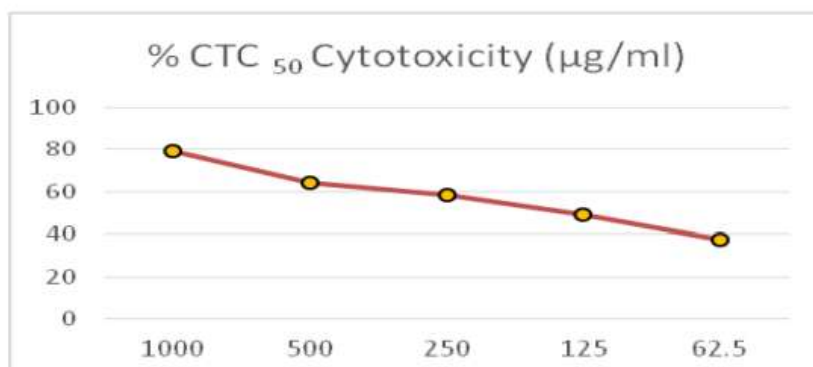
**Table 3:** Inhibition of TNF-α-activated NF-κB and NO production

**FIGURE:**



**Figure 1:** Isowithametelin

**GRAPH:**



**Graph 1:** CTC<sub>50</sub> values of the compound isolated from the ethyl acetate fraction of Datura stramonium flowers against human Liver cancer HePG2 Cell line.

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