

## The anticancer effects of different species of *Cynanchum*

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### Abstract

The prevalence of cancer is increasing worldwide. Oxidative stress and chronic inflammation or disturbance in signaling and metabolism lead to an increase in diseases such as cancer, diabetes, and cardiovascular diseases. Oxidative stress caused by excessive production of free radicals and reactive oxygen species (ROS) disrupts cell function, including general changes in the cellular system, followed by the development of cancerous tumors. Today, many drugs and chemical methods have been discovered for cancer. However, no effect of plant compounds in the treatment and prevention of cancer can be ignored. In this review article, we will examine several *cynanchum* plant species and their action mechanism as anticancer drugs.

**Keywords:** Antioxidant, Breast cancer, *Cynanchum* plant, Plant medicine

### 1- Introduction

Cancer in the 21st century is one of the prime societal and economic problems, accounting for nearly one death in six (16.8%) and one in four death rates from Non-communicable diseases (NCDs) worldwide. Although there have been striking improvements in prevention and therapy, cancer remains one of the most common causes of death, particularly in elderly patients [1]. Breast cancer is one of the most common diseases in females; this may be attributed to the overexpression of a wide range of oncogenes, including HER2/neu [2].

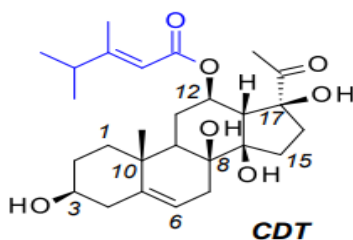
Of these, in men, prostate cancer was most frequent in diagnosis, followed by lung, lip and oral cavity, and liver cancers [3].

Cancer is a genetic disease that arises from gene abnormalities that control cell growth and division, giving rise to cancerous cells. Only about 5-10% of cancers are caused by inherited gene mutations in families. These are called hereditary cancers [4]. The most common hereditary cancer syndromes are caused by mutations in genes like BRCA1, BRCA2, and APC, which increase the risk for breast, ovarian, and colorectal cancers, among others. Most cancers are sporadic because genetic alterations leading to progressives occur randomly during an individual's lifetime and not a consequence of inherited mutations. These are considered non-hereditary or "sporadic" cancers [5].

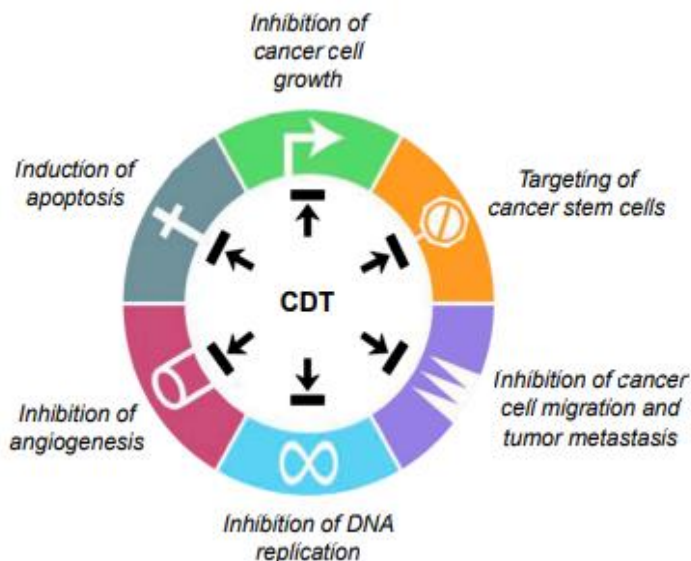
In addition to hereditary cancers, some cancers can also be caused by environmental and lifestyle factors [2].

The history of human use of plants as medicine has yet to be discovered, but gradually and with experience, the information obtained has been passed from one generation to another. From the middle of the 20th century, chemical drugs gave way to medicinal plants, so this century is the peak of the use of medicinal plants. Also, plants have been used as anticancer drugs due to their bioactive compounds, such as phenolic compounds, flavonoids, and alkaloids, which can modulate proliferation and apoptosis factors to prevent tumor growth [6]. Many chemical drugs against cancer have been identified, and chromatin has been identified as an essential target for many anticancer drugs because both chromatin compounds, DNA, and its associated histone proteins participate in this binding process [7]. However, approximately 60% of drugs currently used to treat cancer are derived from natural products [6].

The genus *Cynanchum* of the family Asclepiadaceae comprises over 200 widely distributed species, of which 17 have recently been recognized as medicinal plants. Plants are rich in natural products, especially steroidal glycosides. The C21-steroidal compound caudatin (CDT) "Fig. 1". can be found in different *Cynanchum* plant species. Some species of *cynanchum* that have (CDT) are *Cynanchum auriculatum*, *Cynanchum bungei*, *Cynanchum paniculatum*, *Cynanchum otophyllum*, and *Cynanchum wallichii* Through the following mechanisms, they show anticancer effects "Fig. 2".[8].



**Figure 1: The structure of caudatin (CDT,  $C_{28}H_{42}O_7$ , MW: 490.6 g/mol), which can be isolated from various *Cynanchum* plant species. The tetracyclic aglycone deacylmetaplexigenin is in black and the C-12 ikemaoyl unit is in blue. The numbering scheme is indicated [8].**



**Figure 2: Caudatin has been reported to interfere with many cancer markers, inhibit various types of signaling pathways, and processes related to cell proliferation and metastasis [8].**

In this article, we study the anticancer properties of several species of plants of this family.

## 2- Methodology

Articles related to the anticancer effects of different species of *cynanchum* were studied and reviewed from 2014 to 2024 by searching various databases such as Scopus, PubMed, BioRxiv, and Google Scholar.

## 3- Results

*Cynanchum auriculatum* is a species of climbing vine native to parts of Asia. The extracts from the root of *Cynanchum auriculatum* showed antitumor activity against human hepatocellular carcinoma cell lines HepG2 and SMMC-7721[8]. CDT isolated from *Cynanchum auriculatum* inhibits the formation of breast cancer stem cells by modulating the GR/YAP signaling pathway; CDT also suppresses uterine cancer cells by regulating the TNFAIP1/NF- $\kappa$ B signaling pathway [9].

*Cynanchum paniculatum* (CP) is a medicinal plant with anticancer potential, especially against breast and pancreatic cancer cells. The biological properties provided by CP are through bioactive polyphenolic compounds formed in different parts of the

plant. Paeonol induces breast cancer cell apoptosis by regulating Bcl-2/Bax/caspase3 signaling or CXCR3-B/CXCL4 signaling. Paeonol cooperates in reducing the growth of breast cancer cells by inhibiting PARP, Bax, and caspase-3, as well as by inhibiting p38/JNK/ERK MAPKs [10]. Antioxidants are chemical compounds that delay or prevent the formation of free radicals. Also, by inhibiting cell proliferation, maintaining the normal regulation of the cell cycle, and inducing apoptosis, they prevent the development of cancer [11]. Stigmasterol, a polysaccharide extracted from CP, leads to antioxidant activity and anti-cancer effects through the above mechanism [12].

*Cynanchum acutum* plant species include 2900 species scattered among 348 genera. This plant has needle-shaped leaves and flowers "Fig. 3". Plants belonging to this genus are used as antipyretics, antitussives, diuretics, and pain relievers, whose therapeutic properties have been of interest to researchers in the past. The isolated compounds include six flavonoid compounds identified as rutin (1), quercetin-3-O-neohesperidoside (2), quercetin-3-O- $\beta$ -galactoside (3), isoquercitrin (4), quercetin (5), and kaempferol 3-O- $\beta$ -glucoside (6), besides to a coumarin, is scopoletin (7)[13].



**Figure3:** *Cynanchum acutum* with needle-like leaves and pink flowers[14].

*C. acutum* L. extract can be considered in treating lung and breast cancer. The extracts showed high anticancer effects on lung cancer cell line (A549) and breast cancer cell lines (MCF-7)[15]. It also showed that flavonoids modulate the NF- $\kappa$ B pathway and regulate the expression of miR-146a, thereby exhibiting anti-inflammatory and anticancer mechanisms[13].

### 3- Conclusions

Various factors, including genetic reasons, environmental reasons, and unhealthy lifestyles, can cause the production of cancer cells in the body. Today, with the increase in cancer incidence in different countries, all societies need awareness and proper prevention to control cancer disease. However, medicinal plants can be a positive point in the treatment and sometimes control of various cancers due to their availability of suitable active compounds. By affecting different metabolic pathways, these compounds can control the production of free radicals and adjust the systems. Metabolism can play a role in cancer treatment; although it cannot replace chemical treatment methods, they can have positive and promising effects on cancer prevention.

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