# UNLEASHING THE THERAPEUTIC POTENTIAL OF ANIMAL KINGDOM: A COMPREHENSIVE REVIEW ON ANTICANCER DRUGS DERIVED FROM ANIMALS

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**Abstract**
Animal-derived anticancer drugs have been used in cancer treatment for many years. These drugs are derived from various animal sources such as marine organisms, amphibians, snakes, and mammals. They have shown promising results in the treatment of various types of cancers, including leukemia, lymphoma, breast cancer, and lung cancer. Many of these drug's work by inhibiting cell division or inducing apoptosis in cancer cells. They have also been shown to have fewer side effects compared to conventional chemotherapy drugs. However, the development of animal-derived anticancer drugs faces various challenges, including the limited availability of the sources, ethical concerns, and difficulties in isolating and synthesizing the active compounds. Here in this review bleomycin, cytarabine, eribulin, and ziconotide of animal derived anticancer drugs were discussed in detail. Nonetheless, continued research in this field has the potential to lead to the discovery of novel and effective anticancer drugs from animal sources.

**Keywords:** Anticancer, Bleomycin, Cytarabine, Eribulin, Ziconotide.

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## INTRODUCTION:

Cancer is a leading cause of death worldwide, accounting for approximately 10 million deaths in 2020. The treatment of cancer includes surgery, radiation therapy, chemotherapy, and targeted therapy [1]. While these therapies have been effective, they can cause significant side effects, and some cancer types are resistant to treatment [2][3]. This has led researchers to look for alternative treatments, including natural compounds found in plants and animals [4].

Anticancer drugs derived from animals refer to drugs that are isolated from animal sources, and have shown efficacy in the treatment of cancer [5]. Animals are a rich source of bioactive compounds, including those with potential anticancer properties [6]. Several anticancer drugs derived from animals have been discovered and developed, and some of them are in clinical use. It's important to note that while animal-derived anticancer drugs have shown great promise in the treatment of cancer, their production is often limited due to the complex and time-consuming process required to isolate and purify the compounds from the natural sources [7]. Furthermore, the production of these drugs can have significant environmental impacts, particularly in the case of marine-derived compounds [8-10]. In this review, we will focus on animal-based compounds with anticancer properties.

### Marine Compounds:

Marine animals, including sponges, corals, and mollusks, have been found to contain compounds with anticancer properties [11]. One example is the sponge-derived compound Discodermolide, which has been shown to be effective against a range of cancer types, including breast, lung, and ovarian cancer [12]. Another marine compound, Bryostatin 1, has shown promise in treating lymphoma and leukemia [13][14].

### Venom-based Compounds:

Venom from various animals, including snakes and scorpions, contains compounds that have shown potential as anticancer agents [15][16]. For example, the venom of the Brazilian pit viper contains a protein called Bj-PRO-5a that has been shown to be effective against prostate cancer cells [17]. Similarly, a peptide from the venom of the scorpion *Heterometrus laoticus* has been found to be effective against lung cancer cells [18].

### Animal-derived Proteins:

Animal-derived proteins, including antibodies and enzymes, have been developed as anticancer agents [19][20]. For example, the antibody Trastuzumab (Herceptin) is used to treat HER2-positive breast cancer [21]. Enzymes such as L-asparaginase and Pegaspargase are used to treat leukemia and lymphoma by breaking down the amino acid asparagine, which is necessary for the growth of cancer cells [22][23].

### Animal-derived Hormones:

Animal-derived hormones have also been used as anticancer agents [24][25]. For example, estrogen receptor antagonists, including Tamoxifen and Fulvestrant, are used to treat breast cancer [26-28]. Luteinizing hormone-releasing hormone agonists, including Leuprolide and Goserelin, are used to treat prostate cancer [29][30].

### Animal-derived Peptides:

Animal-derived peptides, including those found in milk, have been found to have anticancer properties [31]. For example, a peptide called Casein alpha S1 has been shown to inhibit the growth of colon cancer cells [32]. Another milk-derived peptide, Alpha-lactalbumin, has been found to be effective against a range of cancer types, including colon, prostate, and breast cancer [33][34].

Here are some examples of animal-derived anticancer drugs:

### Cytarabine:

This drug is derived from a marine sponge, *Cryptotethya crypta* [35][36]. It is used in the treatment of leukemia and lymphoma. Cytarabine, also known as Ara-C (Arabinosylcytosine), is a chemotherapy drug used in the treatment of various types of cancers, particularly leukemia and lymphoma [37]. It belongs to the class of drugs called antimetabolites, which interfere with the DNA synthesis and cell division of cancer cells. Cytarabine is a nucleoside analogue, which means that it mimics the structure of a normal nucleoside molecule, the building blocks of DNA. Once it enters the cancer cell, it gets converted into its active form called cytosine arabinoside triphosphate (ara-CTP), which gets incorporated into the DNA of the cancer cell, leading to abnormal DNA synthesis, DNA damage, and ultimately, cell death [38].

Cytarabine is commonly administered through injection into the vein (intravenously) or directly into the cerebrospinal fluid (intrathecally). It can also be given orally in some cases [39]. The dosage and duration of treatment depend on the type and stage of cancer, as well as the patient's overall health and response to the drug. While Cytarabine is effective in killing cancer cells, it can also cause

side effects, some of which can be severe. Common side effects include nausea, vomiting, hair loss, mouth sores, fatigue, and low blood cell counts [40]. More serious side effects include liver and kidney damage, lung problems, and neurological effects, such as confusion, seizures, and coma. Patients undergoing Cytarabine treatment are closely monitored for any signs of adverse effects [41].

Cytarabine is often used in combination with other chemotherapy drugs or radiation therapy to increase its effectiveness. It has been shown to be particularly effective in the treatment of acute myeloid leukemia (AML), a type of cancer that affects the bone marrow and blood cells. Cytarabine is also used to treat other blood cancers, including acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), and non-Hodgkin's lymphoma [42].

***Structure of Cytarabine:***

Cytarabine, also known as cytosine arabinoside or Ara-C, is a chemotherapy drug used to treat leukemia and lymphoma. Its chemical formula is $C_9H_{13}N_3O_5$, and its molecular weight is 243.22 g/mol.

The structure of cytarabine consists of a pyrimidine base, cytosine, linked to a ribose sugar molecule, which is then linked to an arabinose sugar molecule. The arabinose sugar has a hydroxyl (-OH) group in the 2' position instead of the ribose sugar's usual -H, which makes cytarabine an analogue of natural nucleotides [43].

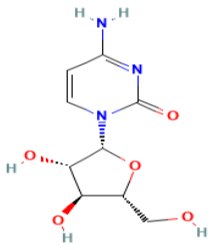

**Fig 1:** 2D Structure of Cytarabine

The two cyclic sugars form the furanoside ring, which gives the molecule its characteristic structure. The nitrogenous base cytosine is attached to the first carbon atom of the ribose sugar, and the arabinose sugar is attached to the fifth carbon atom. The hydroxyl (-OH) group on the second carbon of the arabinose sugar can undergo phosphorylation by the enzyme deoxycytidine kinase to form cytarabine triphosphate, which is the active form of the drug [44].

**Eribulin:**

This drug is derived from a marine sponge, *Halichondria okadai* [45]. It is used in the treatment of metastatic breast cancer. Eribulin, also known by its brand name Halaven, is a chemotherapy drug used to treat certain types of cancer [46]. It is a synthetic derivative of the marine sponge *Halichondria okadai*, and it works by inhibiting microtubule dynamics, leading to the disruption of cell division and subsequent cancer cell death. Eribulin is primarily used in the treatment of metastatic breast cancer, particularly in patients who have previously received at least two other types of chemotherapy. It has also been approved for the treatment of liposarcoma, a type of soft tissue sarcoma [47].

The drug is administered intravenously, typically once every 21 days. The dosage is calculated based on the patient's body surface area, which is a measure of the body's total surface area and is used to determine the appropriate amount of drug to administer. Like most chemotherapy drugs, eribulin can cause a range of side effects. Common side effects include fatigue, nausea, vomiting, constipation, diarrhea, hair loss, and a decrease in white blood cells, which can increase the risk of infection [48]. Other potential side effects include peripheral neuropathy (nerve damage), muscle pain, and a decrease in heart function. Patients receiving eribulin should be closely monitored for signs of these and other potential side effects. Because eribulin can cause harm to a developing fetus, it should not be used during pregnancy. Patients who are breastfeeding should also avoid eribulin, as it can be excreted in breast milk and may harm a nursing infant [49].

***Structure of Eribulin:***

Its chemical name is eribulin mesylate, and its molecular formula is $C_{40}H_{59}NO_{11}$. The structure of eribulin is complex and consists of several distinct components. At its core is a large, highly oxygenated macrocycle, which is connected to a long, branched alkyl chain. The alkyl chain terminates in a highly polar group containing a tertiary amine and a sulfonic acid functional group [50].

The macrocycle contains several functional groups, including a carbonyl, a hydroxyl, and two ether linkages. These functional groups are important for the drug's mechanism of action, which involves disrupting the microtubule dynamics of cancer cells. Overall, the structure of eribulin is highly complex and reflects the molecule's unique mechanism of action and high potency against certain types of cancer [51].

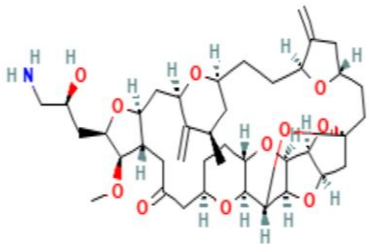

**Fig 2:** 2D Structure of Eribulin

***Ziconotide (Prialt):***

This drug is derived from the venom of a sea snail, *Conus magus*. It is used in the treatment of severe pain, including cancer pain. Prialt, also known as ziconotide, is a medication used to treat chronic pain in patients who have not found relief with other treatments. It is a synthetic form of a peptide found in the venom of a cone snail called *Conus magus* [52].

Prialt is administered through an intrathecal pump, which delivers the medication directly into the spinal fluid through a small catheter that is implanted under the skin. This allows for targeted delivery of the medication to the site of pain, while minimizing the potential for side effects [53]. Prialt works by blocking the N-type calcium channels in the spinal cord, which are involved in transmitting pain signals to the brain. By blocking these channels, Prialt can effectively reduce the transmission of pain signals, leading to relief from chronic pain. Prialt is typically used as a last resort for patients who have not found relief with other treatments, such as opioid pain medications, nonsteroidal anti-inflammatory drugs (NSAIDs), or other analgesic medications. It is also used in patients who are unable to tolerate these other medications due to side effects or other complications [54].

Prialt is known to have a number of potential side effects, including nausea, dizziness, confusion, and difficulty concentrating. In rare cases, it can also cause serious side effects such as seizures, hallucinations, and respiratory depression. Due to the potential for serious side effects, Prialt is only available through a restricted program called the Prialt REMS (Risk Evaluation and Mitigation Strategy) program [55]. This program requires healthcare providers to complete training and certification before prescribing Prialt, and patients are required to sign a consent form before starting treatment. Prialt is a medication used to treat chronic pain that has not responded to other treatments. It works by blocking the N-type calcium channels in the spinal cord, and is administered through an intrathecal pump. While it can be effective in reducing pain, it also has a number of potential side effects and is only available through a restricted program. Patients considering Prialt should discuss the risks and benefits with their healthcare provider [56].

***Structure of Ziconotide***

The structure of Ziconotide is a complex peptide with a molecular weight of 2639.5 Da. It contains 25 amino acid residues, including four disulfide bridges that are important for stabilizing the peptide's structure [57]. The four disulfide bridges in Prialt are formed between the cysteine residues at positions 1 and 4, 8 and 15, 12 and 21, and 16 and 23. These disulfide bonds play a crucial role in maintaining the structure and stability of the peptide, as they create a compact and rigid structure that is resistant to enzymatic degradation [58].

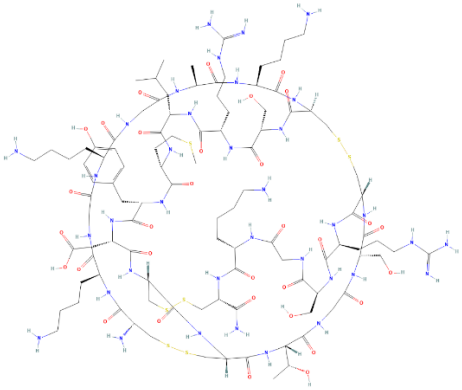

**Fig 3:** 2D Structure of Ziconotide

These drugs work by various mechanisms, such as inhibiting DNA synthesis, disrupting microtubule formation, or inducing cell death. Many animal-derived anticancer drugs have been found to be highly effective against cancer cells, while having relatively low toxicity to normal cells [59].

***Bleomycin:***

This drug is derived from a bacterium, *Streptomyces verticillus*. It is used in the treatment of Hodgkin's lymphoma, testicular cancer, and other types of cancer [60]. Bleomycin is an antitumor antibiotic that was first discovered in the early 1960s. It is produced by the bacterium *Streptomyces verticillus* and is used primarily in the treatment of various types of cancers, including testicular cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, and squamous cell carcinomas [61].

The mechanism of action of bleomycin involves its ability to bind to and break down the DNA molecule, leading to cell death. Specifically, bleomycin binds to DNA and causes the formation of free radicals, which damage the DNA strands. This damage triggers a cascade of events that

ultimately leads to cell death. Bleomycin is primarily used in the treatment of various types of cancers, including testicular cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, and squamous cell carcinomas. It may also be used in combination with other chemotherapy drugs to enhance their effectiveness [62]. Bleomycin is administered intravenously, either as a single dose or in multiple doses over a period of time. The dose and duration of treatment depend on the type and severity of cancer being treated, as well as the patient's overall health and other factors. Bleomycin is an effective chemotherapy drug used in the treatment of various types of cancers. However, it can cause serious side effects, especially lung toxicity, which must be monitored closely during treatment [63]. Patients receiving bleomycin should be closely monitored for any signs of adverse reactions and should report any symptoms to their healthcare provider immediately [64].

***Structure of Bleomycin:***

Bleomycin is a glycopeptide antibiotic and antitumor agent. It consists of two main components: the peptide moiety and the bithiazole chromophore. The peptide portion of bleomycin contains a total of 13 amino acids, including several unusual amino acids such as α-aminoisobutyric acid (Aib) and β-hydroxyaspartic acid (Hya) [65]. The chromophore portion of bleomycin is composed of two bithiazole rings connected by a peptide chain. The bithiazole rings are responsible for the DNA-binding and cleavage activity of bleomycin. The chromophore also contains a metal-binding site, which is thought to be essential for bleomycin's ability to cleave DNA [66].

The overall structure of bleomycin is complex and includes multiple rings and chains, making it difficult to depict in a simple linear fashion. However, the basic structure can be summarized as A linear peptide chain consisting of 13 amino acids, A disaccharide moiety consisting of two glucose molecules attached to the peptide chain, Two bithiazole rings connected by a peptide chain and A metal-binding site near the center of the chromophore. The exact structure of bleomycin can vary slightly depending on the source and method of isolation, but the basic components remain the same [67].

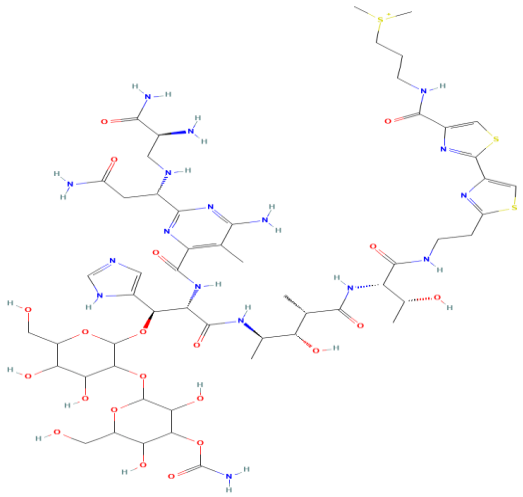

**Fig 4:** 2D Structure of Bleomycin

**CONCLUSION:**

Animal-based compounds with anticancer properties have shown great promise in treating various cancer types. These compounds include marine-derived compounds, venom-based compounds, animal-derived proteins, hormones, and peptides. However, further research is needed to fully understand the mechanisms of action of these compounds and to develop effective therapies that can be used in clinical practice [68]. Nonetheless, these findings provide an exciting avenue for the development of new, alternative treatments for cancer. Animal-derived anticancer drugs have provided a valuable source of new and effective treatments for cancer. Further research and development in this area may lead to the discovery of new drugs with improved efficacy and reduced environmental impact [69].

Animal-based anticancer drugs have played a significant role in the development of cancer therapies. Many of the commonly used drugs such as taxanes, platinum compounds, and anthracyclines have been derived from natural sources, including animals. These drugs have demonstrated promising results in treating various types of cancer, improving survival rates, and enhancing the quality of life for cancer patients. However, as we continue to develop new cancer treatments, it is essential to consider the ethical implications of using animals in drug development. Animal testing has been a controversial issue for decades, and many organizations are advocating for alternative methods to reduce the use of animals in research. Overall, animal-based anticancer drugs have had a profound impact on cancer treatment, but there is still much work to be done in finding

new, effective therapies while ensuring that animal welfare is considered [70].

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