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REVIEW ON THERAPEUTIC POTENTIAL OF SNAKE VENOM AS ANTICANCER THERAPY

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ABSTRACT

One of the main causes of death in the globe is cancer. It is crucial to find new medications made from natural ingredients. The fundamental problem with the way cancer is now treated is that after initial treatments, the disease develops a resistance to medication. As a result, the use of anticancer drugs made from natural sources has increased. The diversity of snake venom is a unique reservoir from which new medicines can be developed. There is a lot of potential for some of the components in snake venom to be used as anticancer drugs. Snake venom contains the toxin, which is a mixture of compounds predominately composed of proteins and peptides. The activation of cytotoxicity, apoptosis, cell cycle arrest, and prevention of metastasis, angiogenesis, and tumour growth are just a few of the anti-tumour properties of snake venom toxins. Here, we discuss the role of crude snake venom and toxins, such as phospholipids A2, L-amino acid oxidase, C-type lectin, and this integrin, as possible anticancer medicines that have been studied in cancer cell lines and animal tumour models and compared to normal cell lines.

KEYWORDS: Cancer, Snake venom, Anti-tumour drug, Carcinogenesis.

INTRODUCTION

In both industrialized and developing nations, cancer is the leading cause of mortality. A Total of 14,61,910 new cancer cases as well as 8,08,000 cancer-related deaths has been reported in the year 2022. Genetic mutations cause variations in the expression, activation, or location of regulatory proteins in the cells in all forms of cancer, changing the signalling pathways that change the cells' responses to regulatory cues and enable unrestrained cell proliferation. Snake venoms are produced in venom glands and are the secretion of deadly snakes.[1] Venom from snakes contains a complex blend of enzymes, poisons, nucleotides, proteinaceous toxins, and peptidyl toxins. Protein makes up about 90% of the dry weight of venom. These proteins could either be harmful or not. A variety of bioactive compounds with pharmacological significance can be found in snake venoms. It is a natural source of numerous active chemicals, including neurotoxic, cardiotoxic, and cytotoxic ones.[2] Venom glands in snakes continuously produce snake venom, which is then harvested using methods and procedures that are based on science. The location, habitat, age, and other factors affect the venom of various snake species. The amount of venom secreted by glands also varies on the season and climate. It is a translucent, viscous liquid that can crystallize when dried. According to their mechanism of action and consequences, snake venom has been divided into three groups: cytotoxins, neurotoxins, and hemotoxins. Heart failure and breathing difficulties are caused by neurotoxins that attack the central nervous system. They can prevent ion transport across the cell membrane and stop neurons from communicating with one another. The poisons that kill RBC are known as hemotoxins. It has an impact on blood and circulatory system processes. It also attacks the host's muscle tissue. Venoms that are cytotoxic target particular cellular locations or muscles. While rattlesnakes and copperheads have hemotoxic venom, cobras, kraits, and sea snakes have neurotoxic venom. When a snake bites its prey, venom is subcutaneously injected, causing both local and systemic consequences. Blood loss and dermo necrosis are two examples of the local effects. Myotoxicity, anticoagulant properties, and hypotension are examples of systemic toxicity. Proteins and membrane components are hydrolyzed by the enzymes found in snake venom, which causes blood clotting and tissue destruction. For the treatment of cancer, numerous methods including chemotherapy, radiation, immunotherapy, and gene therapy have been tried. The treatment of cancer today is extremely difficult everywhere. Chemotherapy, radiation, and surgery are all quite expensive and have a lot of negative side effects. Both normal and malignant cells are impacted by current therapeutic approaches. It results in the identification of

natural cancer treatments. Some elements in snake venom have the power to slow the development of malignant cells. Snake venom works in a way that is similar to how medications work. This characteristic of the venom made it a viable drug product. It will user in a new age for the treatment of cancer, keeping in mind the potential uses of venom in the pharmaceutical industry.[3]

The family, genus, and species of snakes, as well as their geographic region, usual prey species, age, and size, all affect the composition of snake venom. The venom gland's promiscuous secretion of proteins that were previously endogenous proteins with a physiological role elsewhere in the body is a paradigm of how snake venom evolved. If such expression in the venom gland confers an advantage, then this trait becomes fixed and amplified in the venom gland, with secondary specific duplication and diversification of the proteins, leading to multigene families with venom-gland specific expression, toxin neofunctionalization within such families through random mutation, and additional evolutionary selection pressures operating upon their evolution. Consequently, different bioactivities may exist within a single toxin family.[4]

Cancers causes in india:

In India, 23 main malignancies were responsible for 12.85 million fatalities between 2000 and 2019. Mouth and oropharyngeal cancers (15.6%), stomach cancer (10.6%), lung cancer (9.6%), breast cancer (9%), and colorectal cancer (8%) were the most often fatal malignancies. The mortality trend was down 0.19% annually for men and up 0.25% annually for women; a rise of 0.02% was seen for both sexes combined. Lung, breast, colorectal, lymphoma, multiple myeloma, gallbladder, pancreatic, kidney, and mesothelioma cancer deaths increased between 2000 and 2019.[5]

Mortality trends of different cancers from 2000-2019:[6]

Type of cancer	Cases	Percentage	Deaths	Percentage
Breast	178361	13.5	90408	10.6
Lip, oral cavity	135929	10.3	75290	8.8
Cervix uteri	123907	9.4	77348	9.1
Lung	72510	5.5	66279	7.8
Colorectal	65358	4.9	38161	4.5
Oesophagus	63180	4.8	58342	6.9
Stomach	60222	4.5	53253	6.3
Leukemia	48419	3.7	35392	4.2
Ovary	45701	3.5	32077	3.8
Nhl (Lymphoma)	35828	2.7	20390	2.4
Liver	34743	2.6	33793	4.0
Larynx	34687	2.6	21660	2.5
Prostate	34540	2.6	16783	2.0
Brain	31460	2.4	26656	3.1
Hypopharynx	28489	2.2	11443	1.3
AllCancers	13,24,413	-	8,51,678	-

Pancreatic cancer had the biggest annual rise in mortality for both sexes: 2.7% for women, 2.1% for men. Regardless of gender, the mortality rates for malignancies of the stomach, esophagus, leukaemia, larynx, and melanoma were on the decline. The mouth, the cervix uteri, the breast, and the tongue are the top 5 primary locations for cancer in India, with an estimated 13,92,179 individuals expected to be diagnosed by the year 2020.[7]

In 2020, there are expected to be 13,92,179 cancer cases in all of India's states and union territories, according to the National Cancer Registry Programme of the Indian Council of Medical Research (ICMR). This number increased to 14,26,447 in 2021 and to 14,61,427 in 2022.[8]

Year	Total cases	death
2020	13.92 lakh	7.70 lakh
2021	14.26 lakh	7.89 lakh
2022	14.61 lakh	8.08 lakh

There will be roughly 19,58,310 new cases of cancer overall in 2023, or 5370 cases daily. In addition, there will be roughly 89,070 new instances of cutaneous melanoma in situ and 55,720 new cases of ductal carcinoma in situ in women.[9]

Global cancer status:

For 10 nations—Denmark, Ireland, Belgium, Hungary, France, The Netherlands, Australia, Norway, France (New Caledonia), and Slovenia—the age-standardized rate was at least 300 per 100,000. With 334.9 cases per

100,000 persons, Denmark had the highest overall cancer rate for both men and women.

There will be 18.094,716 million new cancer cases worldwide in 2020. The overall age-standardized rate for all malignancies in 2020 was 190 per 100,000 people (excluding non-melanoma skin cancer). Men had a higher rate than women (178.1 per 100,000) (206.9 per 100,000).Hungary had the highest rate, with 371 men being diagnosed with cancer for per 100,000 inhabitants. With 371 men diagnosed with cancer for per 100,000 people, Hungary had the highest rate.

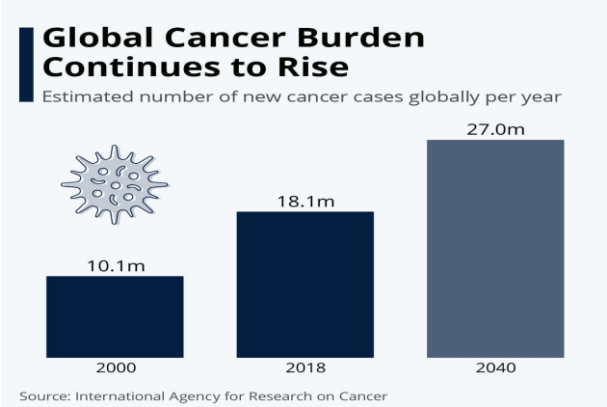

Figure 1: Global cancer burden status estimated number of new cancer cases globally per year. (Source: international agency for research on cancer).

In eight countries—Hungary, Latvia, France, Lithuania, Slovakia, Slovenia, Estonia, and Ireland—the age-standardized rate was at least 350 per 100,000. Denmark had the highest rate of female cancer at 328.3 per 100,000. In four nations—Denmark, Belgium, Ireland, and the Netherlands—the age-standardized rate was at least 300 per 100,000.

Snake venom

Since the 1930s, trigeminal neuralgia, multiple sclerosis, rheumatoid arthritis, asthma, and polio have all been treated using cobra venom. The antibacterial substances L-amino acid oxidase (LAAO) and phospholipase A2 (PLA2) have been identified from snake venom. Venom is only a fluid produced by venomous creatures in a region of their bodies known as the venom gland. [10,11]

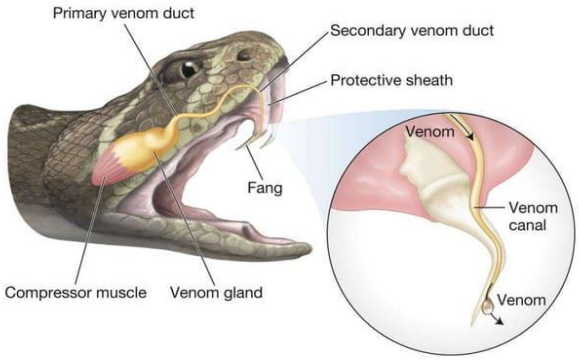

Figure 2: Venom Glands and Fangs of venomous snake.

While members of the Viperidae family including rattlesnakes, copperheads, and cotton heads have hemotoxic, venoms, cobras, mambas, sea snakes, kraits, and coral snakes carry neurotoxic venom. Hemostotoxins and neurotoxins may both be present in some snakes. Snakebites are mostly a rural-area ecological and occupational danger. Snake venom is a mixture of benign proteins, including carbohydrates and metals, and enzymatic and nonenzymatic compounds. The deadly weapons of snakes are made up of roughly 20 poisonous enzymes. In addition to tiny peptides, amino acids, carbohydrates, lipids, nucleosides, biological amines, metal ions, and proteases, the venom contains phosphodiesterase, cholinesterase, hyaluronidase, ATPases, and other toxins. Neurotoxins and cardiotoxins are present in cobra venom. Acetyl cholinesterase and vasculotoxins found in viper disrupt coagulation pathways. Neurotoxin found in the venom of kraits causes presynaptic blockade.[12,13]

Types of snakes and snake venom:

Snakes are categorized as belonging to the Chordata phylum, Vertebrata subphylum, Reptilia class, Squamata order, and Serpentes suborder. The seven families and

subfamilies of poisonous snakes are Colubridae, Elapidae, Hydrophidae, Viperidae, Crotalinae, and Viperinae out of a total of 14.

There are about 60 different poisonous snake species in India, but the 'Big Four' — the spectacled *cobra* (Naja naja), the common krait(Bungarus caerulus*)*, the saw-scaled viper *(*Echis carinatus), and the Russell'sviper (Daboia russelii) — are the most lethal. The WHO refers to snakebites as a neglected tropical disease, and with 50,000 people a year dying from them, India is forced to look into a variety of practical solutions Snakes play important roles in the ecology as predators, prey, ecosystem engineers, and economic and medicinal agents for humans. The sole known treatment for snakebite, known as snake-anti venom, is likewise made from snake venom.[14]

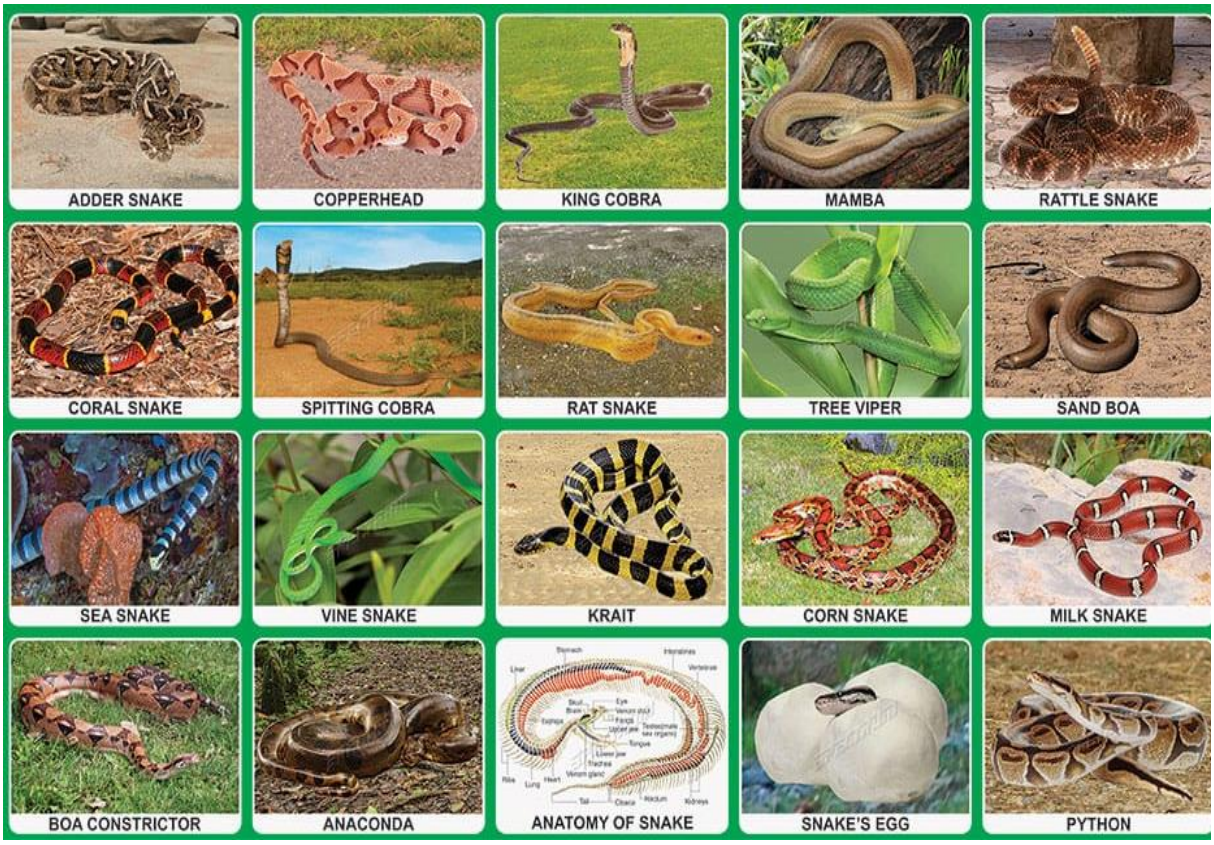

Figure 3: Types of snakes.

The four different forms of snake venom are proteolytic, hemotoxic, neurotoxic, and cytotoxic. Proteolytic venom, which is present in all snake bites, is frequently omitted off the list. The property of venoms are discussed in detail.[15]

Proteolytic venom

The prey's death is hastened by the venom, which also may aid in digesting by rupturing the blood vessel walls and muscle tissue. Rattlesnakes and other pit vipers have a significant amount of proteolytic venom, which combines with their hemotoxic venom to cause severe wounds.The majority of snake venoms contain proteolytic enzymes. The breakdown of tissue peptides and proteins into amino acids is facilitated by these enzymes. Metalloproteases and serine proteases are the two main categories of proteolytic enzymes, which each have a unique way of affecting the haemostatic system.

Example: Rattle snake, Pit vipers.

Hemotoxic venom

Swelling, hemorrhaging, and necrosis are all side effects of hemotoxic venom, which also harms the circulatory system and muscular tissue. Numerous substances found in viper venoms, such as those that support or counteract coagulation, fibrinolysis, platelet activity, and vascular integrity. Venomous creatures, such as snakes (such as vipers and pit vipers) and spiders (such as the brown recluse), regularly use hemotoxins. Animal venoms contain proteins and enzymes that can be hemotoxic, neurotoxic, or even both (as in the case of the Japanese mamushi, the Mojave rattlesnake, and other species like it)

Example: Saw scaled vipers, Levantine viper, Pit vipers.

Neurotoxic venom

Elapid venoms are known to include neurotoxins that have an effect on the nervous system, whereas viperid venoms are known to predominantly disrupt blood coagulation. The majority of cobras, mambas, and kraits have venom that frequently contains neurotoxic

substances. Cobra genus around 300 venomous species, including sea snakes, coral snakes, kraits, and mambas, belong to the family Elapids Elapidae. Short fangs at the front of the upper jaw are used to bite downward, followed by chewing. Their venom can harm blood cells or body tissue, albeit it primarily harms neurons.
Example: Kraits, Mambas, Most cobras.

Cytotoxic venom
The name "cytotoxic venom" refers to venom that kills cells. This venom is less harmful when compared to hemotoxic or neurotoxic venom. However, cytotoxic venom frequently leads to secondary ailments like loss of limb function and other problems.These cytotoxins are prevalent in the venoms of elapids like cobras (Naja), king cobras (Ophiophagus), and most vipers, and can be found in the majority, if not all, toxin families. The biggest poisonous snake in the world is the king cobra (Ophiophagus hannah).[16,17]
Example: Rattle snakes, Puffadders, Cobras

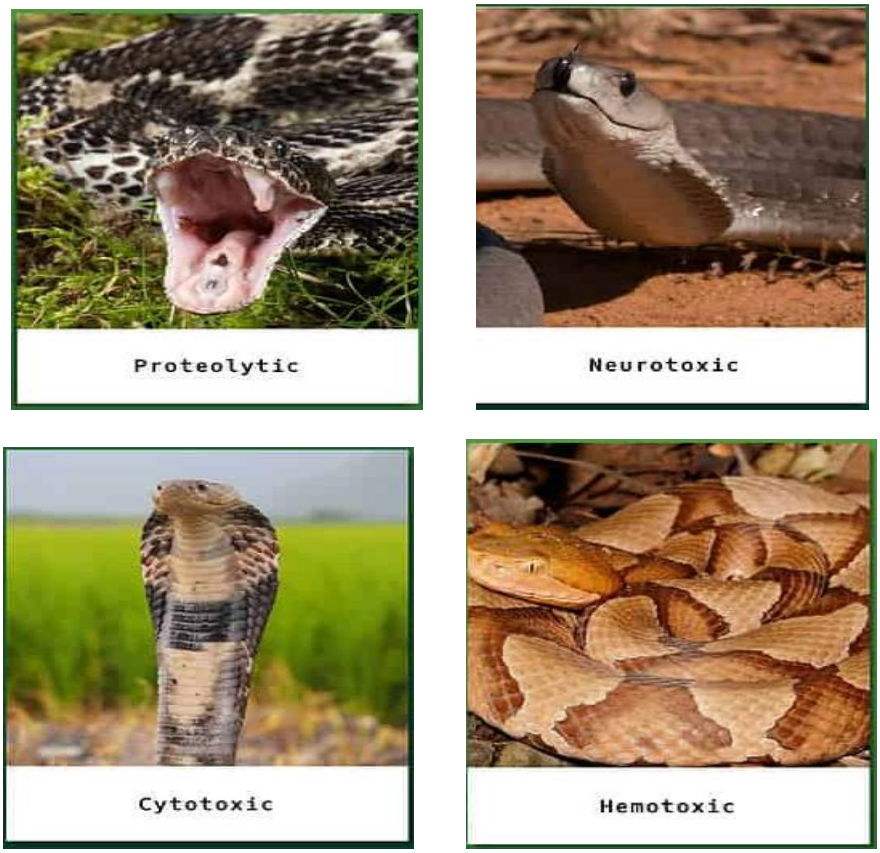

Figure 4: Proteolytic snake, Hemotoxic snake, Neurotoxic snake, Cytotoxicsnake.

Basic components in snake venom
Complex mixtures of peptides, proteins, chemicals, and inorganic cations make up snake venom. Additionally, lipids, free amino acids, and carbohydrates are present in snake venom. At least 25 different enzymes, in varied proportions and combinations, are present in snake venom, but more often than not, they are all present. These enzymes are desirable study models due to their improved catalytic efficiency, thermal stability, and resistance to proteolysis.[18,19]

Hyaluronidase
The beta-N-acetylglucosaminidic links in the HA polymer are broken down by an enzyme called endoglycosidase. It is frequently referred to as the "Spreading factor" in venom. In addition to acting as a spreading agent, it is also necessary as a therapeutic agent to prevent the systemic absorption of venom and to lessen local tissue damage at the bite site. This enzyme's main job is to destroy the extracellular matrix at the bite site, which causes serious morbidity. Proteinaceous hyaluronidase is extracted from snake venom and other venoms. Since they have detectable activity at a pH of about 8, these enzymes are neutral. The testicular enzyme displays *in vitro* transglucosylase activity at a pH of 7. Along with spreading and harming tissue, venom hyaluronidase.[20,21]

L-Amino acid oxidase (Laao)
It makes up 1% to 9% of the total protein in venom. Ophio- amino- acid oxidase is another name for this enzyme. The stereospecific oxidative deaminate ion of a L-amino acid substrate to a matching ketoacid with the formation of hydrogen peroxide and ammonia is catalyzed by the flavoenzymes known as LAAO. This oxidoreductase enzyme is specifically attracted to hydrophobic amino acids. The yellow hue of snake venom is caused by this enzyme. In the families of

Viperidae, Crotalidae, and Elapidae, LAAO are widely distributed.[22]

Phospholipases A2

The richest sources of PLA2 are in the venom of snakes. Snake venom is a complex mixture of active proteins or peptides from calcium ion dependent secretary PLA2, which acts as a defence mechanism by immobilizing the prey and as a digesting enzyme. There are two varieties: 1 PLA2 and 2 PLA2. While 2PLA2 is present in vipers and pit vipers, IPLA2 is only found in cobras, kraits, and sea snakes. Major components of snake venom are phospholipase A2, which exhibits a range of important harmful properties including neurotoxicity, cytotoxicity, cardiotoxicity, hypotensive, and proinflammatory effects.[23]

Cholinesterase

One of the enzymes in snake venom that targets the neurological system is cholinesterase. Exogenous cholinesterase may be a useful therapeutic agent in the management of prophylaxis and organophosphorus poisoning due to its high reactivity towards organophosphorus compounds.[24]

Collagenase

The proteinase enzyme collagenase is designed specifically to break down collagen. Mesenteric collagen fibres are broken down by the collagen found in snake venom.[25]

Thrombin

Plasma clotting is caused by fibrinopeptides A and B that are released by thrombin.[26]

Thrombin like enzymes:

These enzymes, which are glycoproteins by nature, clot plasma and purify fibrinogen *in vitro* while acting as anticoagulants *in vivo*. Due of their role as a defibrinating agent, these enzymes have drawn greater attention. Crotalase, ancrod, and batroxobin are a few examples of thrombin-like enzymes that can be isolated from snake venom. In animal burns, catalase is involved in the production of fibrin. The fibrinogen has been eliminated with Ancrod and Batroxobin.[27,28]

Acetylcholinestrase:

It operates as an exonucleotidase, releasing 5 mononucleotides from the polynucleotide chain and altering DNA and RNA functionality. All deadly snakes contain acetylcholinesterase.[29]

RNase

The endopolynucleotidase RNase, which is present, is selective for DNA's pyrimidine containing pyrimidyladenyl linkages.[30]

DNase

This produces oligonucleotides that break the DNA's 3' monoesterified phosaphate link.[31]

Otherenzymes

There have also been reports of proteolytic enzymes, RNase, DNase, polypeptides, and lactate dehydrogenase in various snake venoms.[32]

Collection of snake venom:

Venom collection, also referred to as "milking," is the process of obtaining the harmful fluids needed for studying animal venoms and/or producing venom products. The three main types of venom collection techniques are: involuntary venom extraction (massaging the glands, stimulating them electrically, or administering induction chemicals to encourage venom expulsion); voluntary venom extraction (getting the animal to release its venom voluntarily); and venom gland extraction (surgical aspiration or trituration of homogenized gland tissue). The process of choosing a strategy must take into account the desired venom yield and composition, level of toxin purity, target animal species, animal welfare, human safety (preventing envenomation), and human.[33]

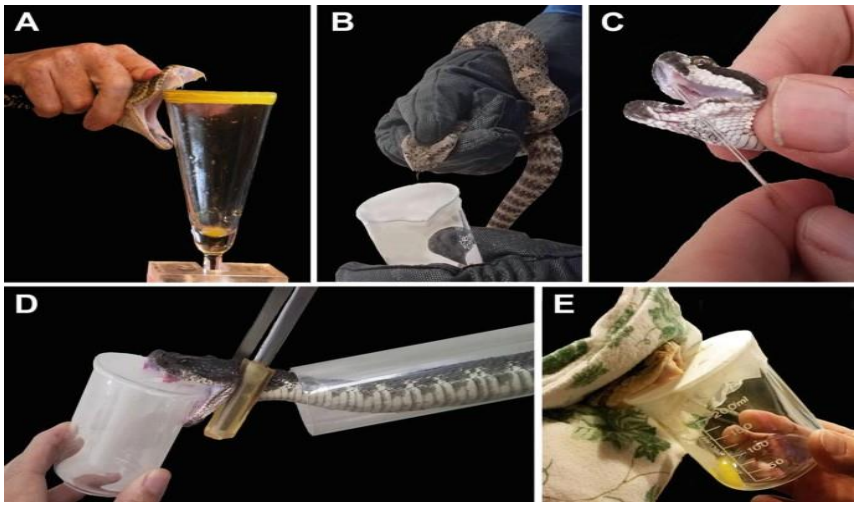

Figure 5: Collection of snake venom extracting venom from snakes a process is milking.

Mechanism of carcinogenesis:

It has been demonstrated that several snake venom toxins cause cytotoxicity against cancer cell lines. The processes by which these poisons carry out their actions, however, are not well understood. Understanding these pathways are essential to furthering this field's research and enabling pre-clinical and clinical evaluation of their potential anti-cancer applications.

Mechanisms of snake venom toxins that are proposed to be cytotoxic to cancer cells. Toxins in snake venom target and interfere with many locations in cancer cells. Damage to the membrane brought on by PLA2, LAAO, and/or 3FTx can activate intrinsic and extrinsic apoptotic pathways. The extrinsic process is fuelled by the connection between an external cell death ligand and receptor, whereas the intrinsic mechanism is mediated by mitochondrial cytochrome C release to the cytoplasm.[34]

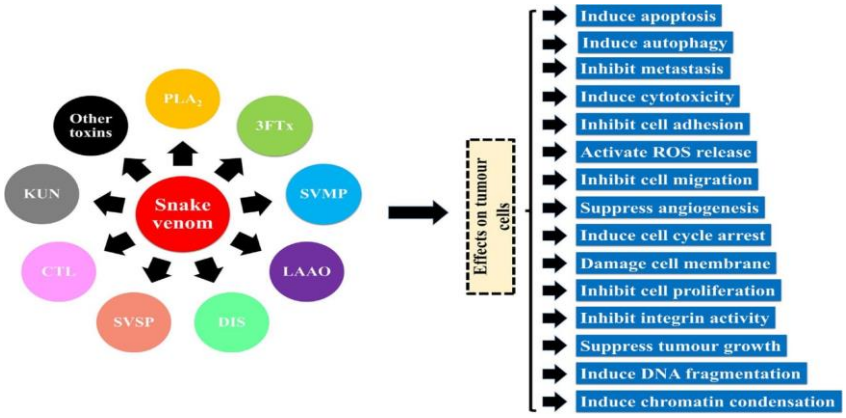

Figure 6: Effects of snake venom and its poisons on cancer cells. Toxins and snake venom affect other physiological systems that control anti-tumour activities as well as the expression or activity of proteins that are specific to tumour cells. Abbreviations: LAAO, L-amino acid oxidase; PLA2, phospholipidase A2; SVMP, snake venom metalloproteinase; SVSP, snake venom serine protease.

As a result of these actions, the caspase cascade is activated, DNA is fragmented, the cell cycle is arrested, Bcl-2 associated X is upregulated; Bcl-2 is down regulated, and so on. Reactive oxygen species (ROS) produced by L-amino acid deamination catalyzed by LAAO can damage cell membranes and subsequently trigger the apoptosis of cancer cells. The catalase enzyme's activity controls the production of ROS. Focal adhesion kinases (FAK), angiogenesis, and actin cytoskeleton remodelling are just a few of the pathways that are inhibited by DIS when it binds to the kindlin- and talin-regulated integrin. Vascular endothelial growth factor (VEGFR) binding by PLA2 can impede cell vascularization, invasion, metastasis, and other processes. Through extrinsic and/or intrinsic mechanisms, other toxins may potentially cause cytotoxicity against cancer cells.[35]

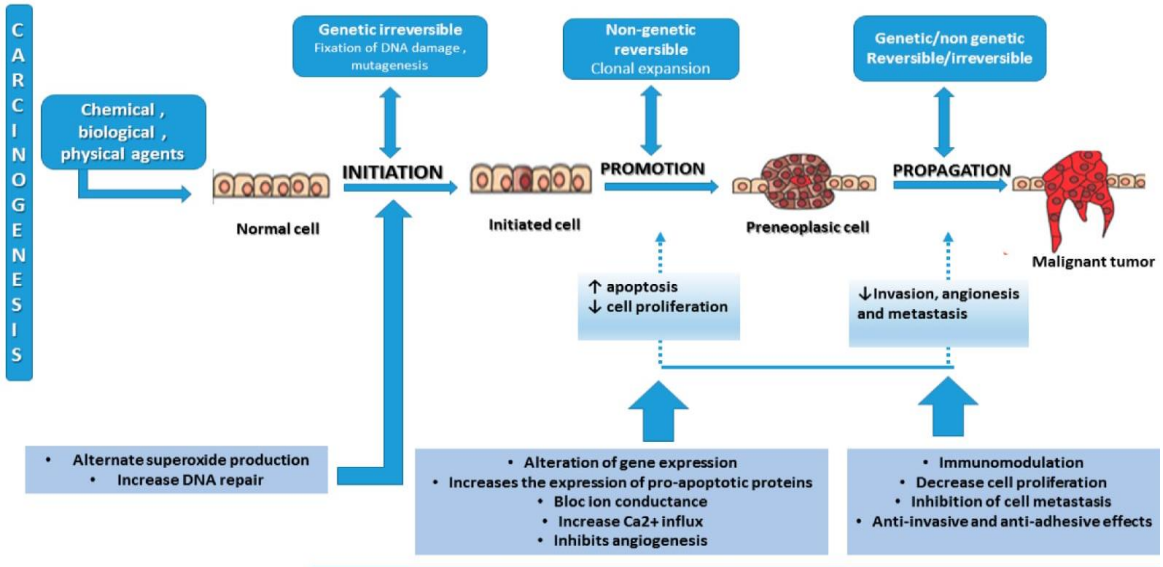

Figure 7: Carcinogenesis and The effects of toxins from snake venom on the different Steps and Process.

Research on their relationship to cancer are based on the characteristics of endogenous lectins produced by tumour cells. They inhibit the proliferation of tumourcells. DNA repair genes are required to fix DNA damage. The presence of other gene mutations and chromosomal abnormalities, such as chromosomal duplications and deletions of chromosomal segments, are frequently found in cells with mutations in these genes. The combination of these changes may cause the cells to become cancerous. Snake venom works by damaging cell membranes, acting as an anti-platelet, preventing fibrin formation, preventing thrombin-induced metastasis, and inducing cancer cells to undergo apoptosis, in addition to increasing Ca2+ influx, cytochrome C release, decreasing or increasing the expression of proteins that regulate cell cycle.[36,37]

Preparation and Storage of snake venom:

Animals are hyper-immunized using venom preparations as part of the antivenom production process, and reference venom samples are provided for routine and/or preclinical antivenom potency testing. Snake venoms are considered beginning materials for pharmaceutical products under GMP, so assuring their quality is essential. Their manufacture should adhere to the following guidelines and principles. The manufacture of venom should adhere to the fundamental principles of quality systems, including traceability, repeatability, taxonomic accuracy, and hygiene control. The WHO's Guidelines on GMP for Biological Products and Guidelines for Good Manufacturing Practices for Pharmaceutical Products should be followed by producers of snake venoms used to make antivenin.[38]

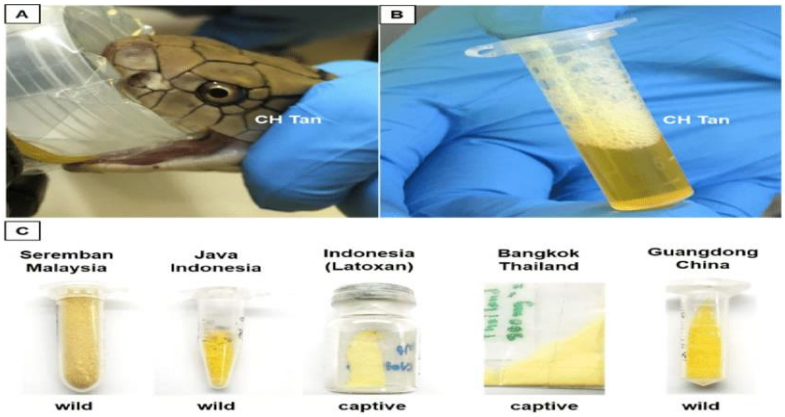

Figure8: Collection of snake venom (A) milking of venom by inducing the snake to bite through a film-covered clean container.(B) Freshly milked venom with its bright golden color.(C) Venom powder in different shades of yellow obtained through lyophilization for long term storage.

The venoms utilized to make antivenom should be typical of the snake population that inhabits the area where the antivenom will be applied. The venom of a sufficient number of individual snakes (often not fewer than 20 specimens, including males and females) gathered from different places encompassing the complete geographical distribution of the specific poisonous snake species must be collected together. There is considerable evidence that age-related venom variation exists within individual specimens and populations, hence it should also be taken into consideration to include venom from juvenile or sub-adult snakes in these venom pools. Antivenom products should be validated by reference laboratories and regulatory bodies or put through preclinical testing by manufacturers using a similar methodology when Standard Reference Venoms (national or regional) are created.[39]

Commercially available snake venom drugs:

In addition to its tendency toward addiction, taking snake venom to get high is exceedingly risky because, well, it's venom! Batroxobin and cobra tide are native substances extracted from snake venoms, and snakes utilize them to paralyze and kill their prey, therefore they don't make for a "safe" recreational drug (although no recreational drug is). The 1981 drug captopril was derived from a component of the venom of the deadly Brazilian viper *(*Bothrops Jararaca*)*. The other medications (bivalirudin, captopril, enalapril, eptifibatide, exenatide, tirofiban, and ziconotide) are synthetic molecules in contrast to the recombinant molecule desirudin.[40,41]

FDA APPROVED DRUGS:

Captoprill

Source: Bothrops jararaca

Pharmacology: Inhibiting angiotensin-converting enzymes**.**

Indication: Hypertension

Aggrastat (Tirofiban)

Source: Echis carinatus

Pharmacology: Glycoprotein 2b/3a inhibitors.

Indication: Heart attack.

Integrilin (Eptifibatide)

Source: Sistrurus miliarus barbouri

Pharmacology: Glycoprotein (GP) 2b/3a inhibitors.

Indication: Acute coronary syndrome.

Defibrase/ Reptilase (Batroxobin)
Source: Bothrops Atrox&B.moojeni
Pharmacology: Converts fibrinogen into fibrin.
Indication: Stroke, pulmonary embolism, deep vein thrombosis and myocardial infarction.

Hemocoagulase
Source: Bothrops Atrox
Pharmacology: Catalyses the coagulation of the blood.
Indication: Plastic surgery, abdominal surgery, and human virectomy.

Exanta
Source: Cobra venom
Pharmacology: Direct thrombin inhibitors.
Indication: Thromboembolic complications of aterial fibrillation**.**

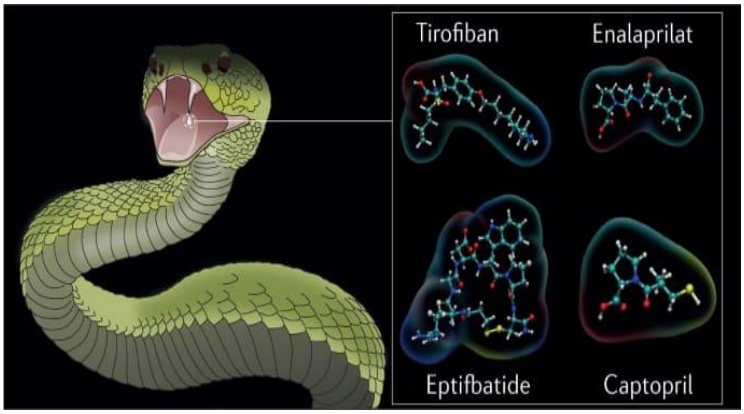

Figure 9: New drugs could be derived from snake venom are proposed.

In clinical trials[42]
Alfimeprase
Source: Agkistrodon contortrix
Pharmacology: Thrombolyticactivity
Indication: Acute peripheral arterial occlusion.

Viprinex
Source: Agkisytodon rhodostoma
Pharmacology: Defibrinogenating agent.
Indication: Acute ischemic stroke.

***In vitro* testing anticancer activity**[43]

Group	Route	Venom	Dose(µg/mice)
1	Subcutaneous	N.haje	2
2	Subcutaneous	N.nig	4
3	Subcutaneous	C.cerastes	6
4	Subcutaneous	Leiurusscorpion	3
5	Subcutaneous	LAO enzyme	50
6	Subcutaneous	Not treated	+(ve)control
7	Intraperitoneal	N.haje	2
8	Intraperitoneal	N.nig	4
9	Intraperitoneal	C.cerastes	6
10	Intraperitoneal	Leiurusscorpion	3
11	Intraperitoneal	LAO enzyme	50
12	Intraperitoneal	Not treated	+(ve)control
13	Notinfected	Not treated	-(ve)control

Role of snake venom as an anticancer agent
Numerous snake venom poisons are studied and turned into medicines to treat diseases like cancer. Generally speaking, the venoms of rattlesnakes and other new world crotalids modify blood vessel resistance, alter blood cells and the coagulation process, and either directly or indirectly alter cardiac and pulmonary dynamics. The nervous system and breathing system could change. The type, quantity, and location of the venom injection determine the strength of the venom and how it affects humans. Other variables including sex, general health, stature, and age also have an impact. Clinical studies and historical evidence indicate that while the majority of deaths happened between 18 and 32 hours, they can happen anytime between 1 hour and several days. Snake venom considerably lowers blood pressure in both experimented-on animals and humans. Snake venom poisoning is connected with hypotension and shock.[44,45]

According to experimental research, an intravenous bolus injection of Crotalus venom results in an instantaneous drop in blood pressure and variable degrees of shock, which are linked to an initial increase

in heme concentration and a subsequent drop in heamatocrit levels. An example of a medicinal made from snake venom is captopril, which is obtained from the venom of the Bothrops jararaca. Increased pulmonary artery pressure, pulmonary artery flow, and blood volume are all observed, along with a rather steady heart stroke volume. An increase in capillary permeability to proteins and RBCs results in hypo volume when Crotalus venom is administered IV slowly over a period of 30 min.[46]

Cancer

Snake venom's cytotoxic action has the potential to obliterate malignant cells right away. Fibrin deposition could create a barrier of protection around the tumour while also halting its growth. Additionally, the fibrin deposits that metastatic tumour cells create may aid in the spread of these tumour cells.[47]

Breast cancer

When coupled with silica nanoparticles (NP), the snake venom from Walterinnesia aegyptia (WEV) can suppress the growth of human breast cancer cell lines and dramatically trigger apoptosis without having a discernible impact on normal breast epithelial MCF-10A cells.[48]

Colon cancer

The prevention of snake venom-induced cell death by hydroxychloroquine, an autophagy inhibitor, shows that snake venom does, in fact, cause autophagic cell death in human colorectal cancer cells.[49]

Prostate cancer

Lebetina turanica, in order to ascertain whether this venom toxin has the potential to function as a therapeutic agent to inhibit prostate cancer cell growth and chemotherapeutic resistance by inducing apoptotic cell death, as well as to ascertain potential processes relating to the inactivation of NF-B signalling.[50,51]

Melanoma

Studies on proteins and peptides generated from snake venom indicate their ability to bind to certain proliferative pathways in melanoma and to block such mechanisms. The combination of these drugs with existing therapies may be the tactical opening that paves the way for the development of more potent melanoma treatments.[52,53]

Other uses of snake venom:

Heart Attacks & Stroke

These drugs thin the blood and dissolve blood clots using proteins. The proteins have also been utilized to dissolve plaque formation in the arteries of people with coronary cardiopathy. It has been discovered that several snakes have proteins that focus on various cancer types. The South Yankee Rattlesnake has been reported to have a macromolecule known as Crotoxin. The macromolecule appears to be particularly drawn to cancer cells and is capable of killing itself.[54,55]

Asthma

Because phosphatidase A and hyaluronidase are antigenic and cause a rise in anti-phosphatidase A, anti-invasin 1, and anti-histamine activity in asthmatic patients, cobra venom is thought to have a positive effect.[56]

CONCLUSION

The goal of the current review is to concentrate on the use of animal venom as a potential source of complementary medicine in the treatment of cancer, which is currently regarded as a serious human illness. Modern researchers anticipate that the biomolecules formed from animal venom are one of the potential sources of natural bioactive substances because it is possible to use these derivatives in biotechnological procedures. The advancement of the biomedical sciences has greatly benefited from studies of animal venoms. Many bioactive compounds, including peptides and enzymes produced from animal venoms, can exhibit significant pharmacological potentialities in human physiology, which can be an efficient tool for reversing the genetic abnormalities seen in malignant cells. In order to use animal venoms clinically for the treatment of human cancer in the future, further study in this area is urgently needed to determine the primary venom components and their precise targets in cell-culture.Numerous studies have been conducted to comprehend the processes that turn a normal cell into a tumour cell due to the necessity to develop new medicines that target genes or pathological pathways. The previous studies states, carcinogenesis is a complicated process that causes a number of changes in a normal cell, including alterations during the initiation, promotion, and progression stages. This process also necessitates important molecular and targeted pathways. This article provides a brief overview of recent developments in this field of study with regard to the active compounds derived from various snake venoms that can be clinically exploited in the treatment of cancer patients, which is currently a major global burden.

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