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REVIEW ARTICLE

Nanoparticle-conjugated animal venom-toxins and their possible therapeutic potential

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ABSTRACT

Nano-medical approaches to develop drugs have attracted much attention in different arenas to design nano-particle conjugates for better efficacy of the potential bio-molecules. A group of promising candidates of this category would be venom-toxins of animal origin of potential medicinal value. Traditional systems of medicine as well as folklores mention the use of venom-toxins for the treatment of various diseases. Research has led to scientific validation of medicinal applications of venoms-toxins and many active constituents derived from venoms-toxins are already in clinical use or under clinical trial. Nanomedicine is an emerging field of medicine where nanotechnology is used to develop molecules of nano-scale dimension, so that these molecules can be taken up by the cells more easily and have better efficacy, as compared to large molecules that may tend to get eliminated. This review will focus on some of the potential venoms and toxins along with nanoparticle conjugated venom-toxins of snakes, amphibians, scorpions and bees, *etc*., for possible therapeutic clues against emerging diseases.

KEYWORDS: Venoms, toxins, nano-technology, nano-particles, nano-conjugation, nano-medicine, therapeutic potential

INTRODUCTION

Advancement in the field of nano-biomedical technology has attracted scientists to explore the domains to conjugate potentially active biomolecules with nanoparticles which can bring forward some cost-effective drugs as future medicine. One such approach would be to conjugate therapeutically potent venom-toxins of animal origin with nanoparticles for their unique properties to enhance their therapeutic value. Bridging nanoparticles with venom-toxins can act as better interface for drug delivery, targeted therapy, and better cellular level interaction thereby increasing the efficacy of the venom toxin bio-molecule having medicinal value.

Venoms are the secretary substances of the venomous animals. Venoms are mixtures composed of a large number of bioactive molecules, such as protein toxins, enzymes, and polypeptides. Toxins are chemically pure, active substances present in the venom that have specific actions on the biological systems. Though venoms-toxins cause patho-physiological conditions but also may turn out to be effective healers of many diseases. As Paracelsus, the 15th century philosopher, had rightly said – "In all things there

is poison; there is nothing without poison. It only depends upon the doses, whether a poison is a poison or not". We now understand that in many cases it is the dose that differentiates a poison from a remedy, which means that any chemical can be toxic if the dose is high, and this is also the basis of modern toxicology. Paracelsus also said that a poison can counteract another and this is the foundation of chemotherapy, antibiotics and immune prevention. It is now well accepted that a poisonous substance could be used as a drug by proper administration, while a life-saving drug might become a poison with indiscriminate use. Use of venoms for treatment of various diseases finds mention in many ancient medicinal texts. In modern day research, detailed studies on the patho-physiological manifestations due to venom and toxin administration, have led scientists to discover logical application of the venom-toxins for developing therapeutically potent agents. Therefore, nano-conjugation of these potential venoms-toxins can provide new insights in developing new drugs and effective treatment.

VENOM TOXINS AS THERAPEUTIC AGENTS

Venom research is being carried out throughout the world for more than 100 years; using snake venom either as medical research tools or directly as therapeutic/diagnostic agent (Pal et al, 2002; Gomes et al, 2010). More than seventy-five years ago, it was proposed that the physiologically active components of snake venom might have therapeutic potential (Calmette et al, 1933). Calmette showed that Cobra venom could treat cancer in mice. Thereafter, many reports have established the anticancer potential of different species of Elapidae, Viperidae and Crotalidae snake venoms (Tu et al, 1974; Iwaguchi et al, 1985; Debnath et al, 2007). Contortrostatin, a toxin derived from *Agkistrodon contortrix*, is an important component showing antineoplastic activity (Zhou et al, 1999), which blocks several critical steps in tumor metastasis including angiogenesis. Recent studies by Park and co-workers reported a toxin from the venom of *Vipera lebetina turanica* that caused apoptosis of human neuroblastoma cells (Park et al, 2009). *dr*CT-I from Indian *Daboia russellii* venom, NK-CT1 from Indian *Naja kaouthia* venom and NN-32 from *Naja naja* venom showed antineoplastic potential against human leukemic cells *in vitro* and EAC bearing mice *in vivo* (Gomes et al, 2007; Debnath et al, 2010; Das et al, 2011). Antiarthritic activity of *Naja kaouthia* venom has also been reported (Gomes et al, 2010). Notexin purified from venom of *Notechis scutatus scutatus* was cytolytic towards neuroblastoma cells SK-N-SH cells via upregulation of Fas and FasL protein expression through p38 MAPK/ATF-2 and JNK/c-Jun pathways (Chen et al, 2010). An enzyme Agkistrodon antithrombogenase (AAT) ameliorated clinical symptoms of rheumatoid arthritis (Cai et al, 2002). Certain cardiovascular drugs from snake venom sources are already in clinical use. Batroxobin, a drug derived from Defibrase purified from *Bothrops moojeni*, has therapeutic application in acute cerebral infarction, non-specific angina pectoris and sudden deafness. Captopril, a drug developed from *Bothrops jararaca* venom, is used to treat kidney disease in diabetes, high blood pressure and heart failure. Recently a novel glycoprotein 1b-binding protein jerdonibitin has been reported from *Trimeresurus jerdonii* venom, which showed potent platelet inhibiting activity (Chen et al, 2011). Gomes and colleagues purified a hexapeptide, Hannahpep, from Indian King Cobra, which showed strong fibrinolytic and defibrinogenating activity (Gomes and De, 1999). They also identified KC-MMTx a 282 D non-protein toxin from the Indian King Cobra venom, which can produce CNS depression (Saha et al, 2006).

Venoms and toxins from amphibian skin also hold promise as medicinal agents like immunomodulatory, cardiotonic, antimicrobial, wound healing, anticancer (Gomes et al, 2007). One mentionable amphibian toxin is the nonopioid analgesic epibatidine isolated from the skin of the Ecuadorian poison frog *Epipedobates tricolor* by Daly and co-workers shows highly potent nicotinic analgesic (Spande et al, 1992) and has longer duration of action than nicotine in analgesia and acts as a nicotine acetylcholine receptor agonist (Qian et al, 1993). It has been suggested that epibatidine is a potent agonist of ganglionic nicotinic receptors and that the alkaloid elicits cardio-respiratory effects similar to those of nicotine (Fisher et al, 1994). Gomes and co-workers identified a non-protein crystal BM-ANF1 and a protein BMP1 that possess anti-neoplastic potential (Gomes et al, 2007; Bhattacharjee et al, 2011) Venoms and purified toxins of invertebrates, particularly the arthropods (including scorpion, centipede, bee and wasp) have been reported to show therapeutic potential. Chlorotoxin, a 36 amino acid peptide from scorpion *Leiurus quinquestriatus* venom, is an effective inhibitor of glioma cell growth. Since it is a high-affinity peptide ligand for Cl- 144 channels and can block small conductance chloride channels, it can interact with chloride channels in membrane protein of glioma cells, thereby preventing trans-membrane chloride fluxes, but this interaction is absent for the neurons and normal glial cells (DeBin et al, 1993; Lyon et al, 2002; Deshane et al, 2003). A synthetic peptide of chlorotoxin named TM-601 has the ability to cross the blood brain barrier and is under clinical trial for treating glioma. Stoppin, a 27 amino acid miniprotein derived from a toxin from venom of Asian scorpion *Buthus martensi* Karsh can kill tumor cells in a p53 dependent manner (Li et al, 2008). Our group identified Bengalin, a protein toxin from Indian black scorpion *Heterometrus bengalensis*, that had selective cytotoxic potential towards leukemic cells U937 and K562 (Das Gupta et al, 2010). Kaliotoxin, a 4kD polypeptide neurotoxin derived from the scorpion *Androctonus mauretanicus mauretanicus* can ameliorate multiple sclerosis and bone reabsorption due to periodontitis, in rat models (Beeton et al, 2001 and Valverde et al, 2004). Mellitin, a 26 amino acid peptide from bee venom, can disrupt cell membrane and enhance phospholipase A2 activity and has various effects on living cells (Mollay et al, 1976; Lad et al, 1979; Cole et al, 1969; Mufson et al, 1979). It possesses potent antimicrobial property (Lubke et al, 1997) and inhibits the growth of the bacteria *Borrelia burgdorferi*, kills *Candida albicans* and suppresses *Mycoplasma hominis* and *Chlamydia trachomatis* infections. Mellitin inhibits hepatocarcinoma cell growth and metastasis (Liu et al, 1964). It also shows anti inflammatory action. Researchers worldwide have identified several other bioactive venom-toxins that were observed to possess certain medicinal properties. However, these molecules need to be properly harnessed and exploited to the fullest, so that they are ready to enter the stage of clinical trials. Here comes the necessity for implementation of new technologies in the field of drug development and nanotechnology is one such application that shows promise in the field of nanomedicine.

NANO-PARTICLES IN NANOMEDICINE

An important application of nanotechnology and nanomedicine is the development of new molecules with nano-scale dimensions for medical applications (Park et al, 2008). Nano-particles act as biological interface between bulk materials and atomic or molecular structures. This technology holds great promise in the field of medical science because of the unique physicochemical properties of nano-particles, such as ultra small size, large surface area-to-mass ratio, high reactivity, and effective interaction with cells, high stability, catalytic power and solubility. These nano-scale materials can be potential candidates of future medicine because of their effective routes of administration, better penetration capacity, lower therapeutic toxicity, efficient and specific target oriented drug delivery system and better interaction at cellular level. Nano-particles have made an impact in the field of medicine by having applications such as biological labelling, drug and gene delivery, bio-detection of pathogens and proteins, DNA and RNA probes, enhancers in optical imaging processes, diagnostics, tissue engineering, separation of biological molecules and cells, combating diseases most importantly in tumour destruction and cancer treatment (Salata et al, 2010). The unique capability of liposomal nano-particles to encapsulate efficiently with different ligands for targeted tissue oriented therapy, prolonged half life period *in vivo*, biocompatibility and specific formulation according to needed specificity makes them potent pharmaceutical carriers (Moghimi et al, 2003; Torchilin et al, 2005). Carbon nano-tubes have been used as drug carriers and nano-devices (Yang et al, 2007). Nano-particles were found to improve contrast in MRI, ultrasound and X-ray techniques thereby bringing new dimensions in bio-imaging techniques (Babes et al, 1999; Liu et al, 2007; Hainfield et al; 2006). Nano-particles, such as liposomes, carbon nanotubes and nano-gold, have been experimentally successful as drug delivery agents (Han et al, 2007). Carbon, fullerene, silicon dioxide, metal oxide, silver, magnesium oxide, zinc oxide, chitosan nanofiber, gold nano-particles have been experimentally proven to posses anti-bacterial properties (Mathews et al, 2010). Silver and gold nano-particles have diverse applications in the field of biology, medical diagnosis and therapy (Sadowski et al, 2008). Dendrimers has also emerged as drug delivery agents due to their unique structural architecture (Bhadra et al, 2003). Super-paramagnetic nano-particles (SPIONs) have been used in magnetic detection and diagnostics (Johnson et al, 2010). Nano-particles conjugated with antibodies have been found to have potent interaction with biological systems (Sidorov et al, 2007). It may be said that nanoparticles have made their remarkable impact and may play a potential role in almost all branches of medical science such as immunology, radiology, oncology, microbiology, orthopaedics, cardiology, ophthalmology and many more (Farokhzad et al, 2006).

Nano-technology has radically changed the scenario of cancer therapy, by providing improved methods of detection, diagnosis, targeted drug delivery, tumour destruction (Kairemo et al, 2008). Research in the field of nano-technology focusing particularly on developments in nanomedicine has been a prime priority throughout the world to bring a new paradigm in the medical arena. In fact, interfacing living cells with engineered nanostructures is needed for biomedical applications for practical therapeutic approach. Hence, nano-technology can be considered a boon to current research since its application can bring forward dramatic changes in medical science.

NANOTECHNOLOGY INSPIRED THERAPY WITH VENOM TOXINS

Nano-particles have unusual properties that can be used to improve the pharmacological and therapeutic properties of drugs. Nanoencapsulation of these therapeutically potent molecules not only provides a media for better drug delivery but also enhance stability, bioavailability and targeted drug application. Larger molecules may get eliminated from the body, but cells take up these nano-particles because of their size. Hydrophylic nano-particles such as chitosan, nano-gold, nano-silver, magnetic and supermagnetic nano-particles, dendrimers, *etc*., are being studied extensively in the role of drug delivery vehicles by conjugating them with several therapeutically potent venoms and toxins, particularly peptides, proteins and antigen.

In addition to its potential in facilitating drug delivery, nano-technology has induced new perspective in therapeutic regime. The concept of smart nano-particle, nano-particle induced hyperthermia (induced by laser in case of plasmonic nano-particle and radio frequency in case of magnetic nano-particle), use of nano rod in sub-cellular targeting (*e.g.*, specific mitochondrial damaged by nano-rod) are some of the examples of this new paradigm of therapy cum diagnostic. The fact that bare nano-particle can alter protein aggregation profile *in vitro* (Singha et al, 2010) as well as *in vivo* in cancer cell shows that the nanoparticles have both toxicological and therapeutic value which cannot be questioned. Similarly, the work by Patra and coworkers shows the cytotoxicity of bare gold nano-particles and that of arginine conjugated gold nano-particle. It has also been shown that the efficacy of an anticancer drug can be improved by several folds by suitable nano-conjugation (Patra et al; 2011; Singha et al, 2011). Behfar and his co-workers have evaluated the antigen delivery potential of chitosan encapsulated *Naja naja oxiana* venom (Mohammadpourdounighi et al, 2010). Chitosan is a hydrophilic biodegradable and non-toxic polysaccharide, which possesses excellent capacity for association with proteins and increased the permeability through cell membranes (Artursson et al, 1994; Dodane et al, 1999) and could enhance the absorption of poorly absorbable drugs (Schipper et al, 1996). By studying the chitosan encapsulation of the *N. n. oxiana* venom, they proposed the possible use of such nanoparticles as an alternative to the adjuvants that are in use currently. Bombesin (BBN) peptides obtained from toad skin showed high affinity towards gastrin releasing peptide (GRP) receptors that are over expressed in prostate, breast and small lung carcinoma *in vivo*. BBN were conjugated with gold nano-particle and also its radiolabelled substitute was developed (Chanda et al, 2010). The constructs exhibited high binding affinity, being GRP-receptor specific, showing high selectivity for GRP-receptor rich prostate tumours in immune-deficient mice and also GRP-receptor rich pancreatic acne in normal mice. The intra peritoneal mode of delivery was found to be effective as the BBN-gold conjugates showed reduced reticulo-endothelial system uptake by organs with concomitant increase in uptake

at tumour targets. A bio-adhesive drug delivery system was developed with wheat germ agglutinin (WGA)-grafted lipid nano-particles for the oral delivery of bufalin (a hydrophobic active component from skin secretion of Chinese toad (*Bufo bufo gargarizans*). It was observed that WGA enhanced the cellular uptake of nano-particles compared with WGA-free lipid nanoparticles thereby indicating that WGA grafted lipid nanoparticles could be a promising carrier to enhance cellular uptake with improved drug bioavailability through the oral route (Liu et al, 2010). Mellitin is a cytolytic peptide and therefore a potential candidate for anticancer therapy. The disadvantages of mellitin are off-target toxicity, non-specificity and unfavourable pharmacokinetics. Soman and co-workers developed a nano-conjugated mellitin where the toxin was incorporated into the outer lipid monolayer of a per fluorocarbon (PFC) nanoparticles (Soman et al, 2009). This nano-carrier allows accumulation of mellitin in murine tumors *in vivo* and significant reduction in tumor growth without any apparent signs of toxicity. The nano-carriers could selectively deliver mellitin to multiple tumor targets through a hemidiffusion mechanism, where the surface membrane was not disrupted but it triggered apoptosis and also caused regression of precancerous dysplastic lesions in animals. By incorporating the mellitin into the nanovehicle, the wide-spectrum cytolytic potential could be restrained and made more specific. To enhance the medicinal activity of bee venom (BV) acupuncture, Jeong and co-workers loaded bee venom into biodegradable poly(d,l-lactide-co-glycolide) nanoparticles (BV-PLGA-NPs) and observed that it could prolong the analgesic effect of PLGA-encapsulated bee venom on formalin induced pain in rats. From the experiments it was evident that PLGA-encapsulation was effective in alleviating the edema induced by allergens in bee venom indicating that PLGA-encapsulation provides a more prolonged effect of BV acupuncture treatment, while maintaining a comparable therapeutic effect (Jeong et al, 2009).

One of the toxins that have been exploited the most by nano-biotechnologists is chlorotoxin from the Israeli scorpion *Leiurus quinquestriatus* venom. Zhang and his group used supermagnetic iron oxide as a nano-vector (Sun et al, 2008) conjugating it with a conventional therapeutic drug methotroxate and a targeting ligand chlorotoxin. Chlorotoxin is known to preferentially target glioma cells over normal brain cells. The conjugated nano-particle resulted in successful attachment of both drug and the chlorotoxin demonstrating preferential accumulation and increased cytotoxicity towards glioma cells. Moreover, prolonged retention of these nano-particles was observed in the tumour cells *in vivo*. In another report Zhang and co-workers developed supermagnetic iron oxide nanoparticle conjugated with an amine-functionalized polysilane and chlorotoxin (Veiseh et al, 2009). It was observed that the nanoconjugation significantly enhanced cellular uptake of the toxin and inhibited cancer invasion by about 98% as compared to unbound toxin (which was about 45%). Chlorotoxin-enabled nanoparticles deactivated the membrane bound matrix metalloproteinase 2 and induced increased internalization of lipid rafts expressing MMP2 and ion channels on its surface, through receptor-mediated endocytosis. Because of the combined imaging capacity as well as therapeutic effects of this nano-conjugated chlorotoxin, it might be a potential candidate for both non-invasive diagnosis as well as treatment for a variety of tumours. Chlorotoxin was used in the development of a magneto fluorescent nano-probe conjugating iron oxide nanoparticle coated with bio-compatible polyethyleneglycol-grafted chitosan copolymer with chlorotoxin and a near-IR flurophore (Veiseh et al, 2009). This nano-probe could traverse the blood-brain-barrier, specifically target brain tumors and leave the blood brain barrier uncompromised. This nano-probe showed innocuous toxicity and sustained retention in tumours.

The MRI detect ability combined with NIRF illumination exhibited by the same nano-probe might allow its use in preoperative diagnostics, tumor resection, and postoperative assessment using magnetic resonance or optical imaging. Sun and co-workers studied the PEG-mediated synthesis process to produce highly stable iron oxide nanoparticle which showed tumor-specific accumulation through both magnetic resonance and optical imaging after conjugation with Chlorotoxin and a near-infrared fluorescent dye [Cy5.5] (Sun et al, 2010). In another study, nano-probes were prepared using polyethylenimine-coated hexagonal-phase NaYF4: Yb, Er/Ce nano-particles and conjugating them with recombinant chlorotoxin to form good biocompatible probes which when intravenously injected into Balb-C mice produced high contrast images when irradiated with near-infrared radiation, indicating highly specific tumor binding and direct tumor visualization. This high sensitivity and high specificity of the chlorotoxin nanoprobe may improve the diagnostic and therapeutic modalities in cancer patients in the near future (Yu et al, 2010).

Recent researches have shown combination of Walterinnesia aegyptia venom with silica nano-particles enhances the proliferative functioning of normal lymphocytes through CXCL12-mediated signaling through PI3K/AKT, NFκB and ERK signalling (Gamal et al, 2012). Dounighi and his co-workers have demonstrated chitosan nanoparticles loaded with *M. eupeus* scorpion venom could be better sustained than with conventional venom loaded adjuvants and therefore, be an alternative option to traditional adjuvant systems (Dounighi et al, 2012). Pornpattananangkul et al reported recently about bacterial toxin enabled drug release from nanoparticle-stabilized liposomes providing new, safe, and effective approach for the treatment of bacterial infections (Pornpattananangkul et al, 2011). There are recent reports by Yu et al claiming rational design of a synthetic polymer nanoparticle that neutralizes a toxic peptide in vivo. The experiments established that the (NPs) accelerate clearance of the toxic peptide and eventually accumulate in macrophages in the liver therefore providing a platform to design plastic antidotes in future (Yu et al, 2011).

Conjugation of venom-toxins with suitable nano-particles would not only provide insights to newer drugs but also better drug delivery systems which would have better therapeutic potential and biocompatibility. Tables 1 provide a list of nano-conjugated venom-toxins; which possess potential to be future therapeutic drugs/diagnostic probes Table 2 therapeutic potential animal venom-toxins for future nano-conjugation.

CONCLUSION

Nature remains the ultimate and major source of infinite biologically active compounds which can bring forward

Table 1. Therapeutically active nanoparticle conjugated venom-toxins.

Therapeutically active animal venoms-toxins	Type of particle used for conjugation	Therapeutic role
Bee venom	Biodegradable poly (d,l-lactic-co-glycolide) (Jeong et al 2009)	Acupuncture
Bombesin peptides	Nano-gold (Chanda et al, 2010)	Anti-arthric
Bufalin	Wheat germ agglutinin (Liu et al, 2010)	Anti-cancer
Chlorotoxin	Supermagnetic iron oxide + methotrexate (Sun et al, 2008) Supermagnetic iron oxide as nanovector (Veiseh et al, 2009) Polyethyleneglycol-grafted chitosan copolymer with near flurophore (Veiseh et al, 2009)	Anti-cancer against glioma Non invasive diagnosis;tumor preoperative diagnostics, tumor resection and post operative assessment
Mellitin	Polyethylenimine-coated hexagonal-phase $NaYF_4$:Yb,Er/Ce nanoparticles (Yu et al, 2010) Grafted lipid nanoparticles of perflurocarbon (Soman et al, 2009)	Diagnostics and anticancer Anticancer
Naja naja oxiana venom	Chitosan encapsulated (Mohammadpourdounighi et al, 2010)	Adjuvent
NK-CT1*	Nano-gold (Gomes et al, Unpublished data)	Anticancer

*Ongoing DBT, Govt of India, sponsored research project in the authors' laboratory

Table 2. Potential venom-toxins for future nanoparticles conjugation.

Potential toxin for future application	Source of origin	Therapeutic role	Target
ACTX-6 (Zhang and Cui, 2007)	*Agkistrodon acutus*	Anti-cancer	A549 cells
Bengalin (Dasgupta et al, 2007)	*Heterometrus bengalensis*	Anti-cancer	U937 and K562 cells
BM-ANF1 (Gomes et al, 2007)	*Bufo melanostictus*	Anti-cancer	Colon cancer and leukemic cells
BMP-1 (Bhattacharjee et al, 2011)	*Bufo melanostictus*	Anti-cancer	EAC cells
Brevinin-2R (Ghavami et al, 2008	*Rana ridibunda*	Anti-cancer	T-cell leukemia (JURKAT)
Bufalin (Zhang et al, 1992)	*Bufo melanostictus*	Anti-cancer	Leukemic and melanoma cells
CTX3 (Dufton and Hider, 1991) (K562)	*Naja naja atra*	Anti-cancer	Leukemic cells
Contortstatin (Zhou et al, 1999)	*Agkistrodon contortrix*	Anti-cancer	Human Breast cancer cells (MDA MB 435)
drCT-1 (Gomes et al, 2007)	*Daboia russeli russeli*	Anti-cancer	Hep G2 cell line
Epibatidin (Spande et al, 1992)	*Minyobates bombetes*	Analgesic	Central Nervous system
Saxatilin (Kim et al, 2007)	*Gloydius saxatilis*	Anti-cancer	Ovarian cancer cells
Stoppin (Li et al, 2008)	*Buthus martensi* Karsch	Anti-cancer	Tumor cells

answers to many unresolved health problems, among which "venom-toxins" are pioneer candidates whose potentiality needs to be unveiled. The realization that venom-toxins are a store house of potential active compounds, which can efficiently interact with highly specific molecular targets are natural sources and not products from chemists test tube give them a better edge in drug development research compared to artificial chemical compounds which shows a new paradigm towards drug development clues. Researchers throughout the world are now showing interests in developing nano conjugated toxins as life-saving drugs, with primary focus on maximizing bioavailability of the drug both at specific places in the body and over a period of time. It is interesting to note that whether nano-conjugation can provide the option of delivering the drug through different routes as per convenience. It has been observed that with development of nano-conjugated venoms-toxins, the therapeutic properties of the drugs improve significantly. Also, site-directed targeting of the molecules may be achieved by nano-venoms-toxins. Larger molecules may get eliminated from the body, but cells take up these nanoparticles because of their size. There is a possibility that due to the nano-conjugation, the nano-particle may act as an alternative to the traditional adjuvant systems, resulting in slow release of the drug to the target site and at the same time lowering the toxicity of the toxins to a large extent. Worldwide research on nanomedicine implies that nano-conjugated venom-toxins hold good promise in the field of drug development and delivery but extensive research is necessary before the nano-based products can be considered for clinical trial. Detailed study is warranted regarding the toxicity profile and bio-distribution of venom-toxin conjugated nanoparticles. The environmental consequences of utilizing the nano compounds should also be taken into

account while considering drug development by nano conjugation. Perhaps, the combination of venom-toxins and nanotechnology can bring forward a revolutionary renaissance in medical science which can set a benchmark in drug development research.

CONFLICT OF INTEREST

None declared.

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