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Modern Medical Research: Potential Use for New Drug Development

Mustafa K*

Department of Pharmacology, Centre for molecular medicine, Turkey

Corresponding author: Mustafa K

kmusta123@fayahoo.co.in

Department of Pharmacology, Centre for molecular medicine, Turkey

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Abstract

In the past 30 years, there has been an exponential growth in highly advanced scientific and medical research technologies, to the point that the large number of identified molecular agents connected to pathogenesis cannot be easily integrated or processed by traditional analytical methods. In fact, the identification of more complex diseases has increased in part as a result of the recognition that various moieties represent disease markers. Thanks to currently accessible cutting-edge technology, researchers and doctors can now examine and analyse any specific dysregulations occurring at the genomic, transcriptomic, miRnomic, proteomic, and metabolomic levels. However, there are limitations to this brave new world of science, including the fact that only isolated molecular levels are now being separately examined for their impact on any given health problem. Systems biology and medicine have mostly focused since their inception in 1992 on the perturbations of overall route dynamics for the start and worsening of the researched condition. Therefore, systems medicine methodologies can be used to shed light on a variety of study settings, ultimately producing the useful finding of novel dynamic interaction networks that are crucial for influencing the course of medical disorders. As a result, systems medicine also helps to pinpoint clinically significant molecular targets for counteracting this illness with diagnostic and treatment methods.

Many of the peptides found in scorpion fluids demonstrated a wide range of biological actions with high specificities to their intended locations. Numerous studies have described their powerful activities against microorganisms and demonstrated their capacity to alter different biological processes related to immunological, neurological, cardiovascular, and neoplastic illnesses. It is predicted that peptides obtained from scorpions could be exploited to create new, specialised medicines because of their significant structural and functional diversity. This review outlines pertinent findings to help make them more effective as useful resources for the creation of novel medicines.

Keywords: Transcriptomic; Drug; Development; Proteomic

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Introduction

The majority of the key molecular determinants thought to affect human situations and diseases may now be examined in great detail thanks to the exponential growth of extremely powerful scientific and medical research analytical tools over the past 30 years [1]. Thanks to developing wet-lab technologies like mass spectrometry, quantitative polymerase chain reaction and next generation sequencing, and comprehensive bioinformatics suites, scientists and clinicians can now start to try investigation of any individual dysregulations occurring within the genomic, transcriptomic, miRnomic, proteomic, and metabolomic levels. These methods can all be used to extract data from large databases, allowing for the creation of disease models that can be tested in wet labs [2]. One of the key contemporary components of clinical research is the interaction between the wet and dry lab

with specialised clinical knowledge. But even in this brave new world of science, there are limitations because, in the majority of cases, just a few molecular levels are individually examined for their potential to affect a certain health issue [3]. Any type of medical research that aims to identify dysregulated molecular pathway connections ought to ideally concentrate on looking at the whole picture of the complicated, multivariate medical illness. Examining all concurrent molecular interactions occuring at various levels requires careful and deliberate consideration. Such "bigger-picture" research viewpoints help researchers gain a deeper understanding of complex and multifactorial disease conditions and, in the end, "fast-track" the clinical diagnosis of particular molecular pathway dysregulations with pathogenesis value as well as the identification of novel drug targets [4]. Natural products have recently received a lot of attention due to their contributions to fundamental studies that aim to find novel medications. According to a 2004 review by Clardy and Walsh, 23% of newly developed medications with FDA approvals were based on naturally occurring chemicals [5]. Toxins with high specificity to target biological components are sought after in this issue in an effort to treat a variety of ailments. Outlining these drugs' Pharmacognosy is necessary to maximise their contributions as therapeutic instruments. In the past few decades, scorpion-derived peptides have been identified, purified, and the focus of significant study due to their abilities to target various ions channels and cell membrane components. There are 800 isolated, identified, and physiologically active native and recombinant polypeptides in these spider secretions [6].

Application of the advent System Medicine [7]

The classic reductionist approach to medical research has been explored and can be limited to the examination of the biological effects of single or minute amounts of crucial molecular actors for complex, multidimensional human illnesses, including cancer. Systems medicine, a notion that dates back to 1992, is the use of systems biology within the scope of contemporary medical research. With such a broad view, it is possible to perceive and gain insight into the holistic character of these illness situations, concentrating primarily on the changes in overall pathway kinetics that lead to the beginning and/or worsening of the condition(s) under investigation. Whenever such a strategy is used, systems medicine necessitates the employment of various crucial components in order to achieve its therapeutic theranostic objectives.

Medicine Implication in Drug Development and research

Prediction of adverse medication effects throughout the early stages of the drug development process is one of the main research challenges where systems medicine approaches can make a significant difference. Pharmacogenetics research for drug development has historically concentrated almost entirely on the role that polymorphisms in individual genes play in creating a particular adverse effect. A systems-based analysis can be much more successful in identifying and/or anticipating damaging adverse effects before any unique lead molecule advances any further along the drug development pipeline, despite the fact that such adverse effects are likely the result of multifactorial influences. The prediction of drug target interactions is an area of research where systems techniques are important. The human ether-a-go-go related (hERG) potassium channel, which is crucial in the control of tumour cell proliferation and death, can be inhibited by new inhibitor compounds that are predicted by the drug-induced gene expression profiles. The Connectivity Map (CMap) was used in this investigation, together with analytical techniques from databases of experimental datasets for annotated hERG inhibitor actions, to choose prospective hERG inhibitors with similar gene signature expression profile induction. System design healthcare techniques also play a key role in the developing field of drug repositioning, where treatments that are thought to be outdated or ineffective for one specific medical disease may instead turn out to be extremely successful for a completely new ailment. In order to examine and reduce drug off target effects for key cancer-signaling pathways, the study concentrated on the investigation of transcriptome expression profiles happening before and after medication delivery.

Vernacular and Toxicology

Over 1500 distinct scorpion species have been identified and documented. The old and new world scorpions are two distinct groups that these arachnids are separated into historically, along with their geographic distribution. In general, the formers are found in Southern America, Asia, and Africa. They form a single family known as the Buthidae, which includes species with triangular-shaped sterna. Although they have a sternum with a pentagonal shape, new world scorpions are extensively distributed across Europe, Asia, and America. The Chactidae suborder consists of six distinct families (Scorpionidae, Diplocentridae, Chactidae, Vaejovidae, Bothriuridae, and Chaerilidae). The Buthidae family has the majority of harmful species, it is important to note. The Chactidae scorpions produce cellular lytic and cytotoxic substances, in contrast to Buthidae animal species that secrete strong mammalian-neurotoxic compounds.

Scorpions Venoms

Polypeptides, nucleotides, lipids, mucoproteins, biogenic amines, and other unidentified compounds are all mixed together in scorpion venom. The quantity of the chemicals produced can vary depending on the animal specimen and the number of stings (and eventually of extractions). Particularly, there are less derivatives of scorpion having enzymatic activity. No more than 5% of the dried weight of the venom was made up of total peptides. This subset includes polypeptides that are frequently categorised into different classes based on their structures, targeting locations, pharmacological relevance, and toxicities for mammals and/or insects and crustaceans. Only 1% of the estimated 100 000 or more bioactive peptides extracted from scorpion venom have been extensively studied. Of these, a wide variety of bioactive peptides have already been isolated and described [8].

Antimicrobial Activity

The majority of research focuses on neurotoxins, which are peptides that disrupt ion traffic across the cell membrane.

They were split into distinct subfamilies according to their toxicity and pharmacological importance. Our understanding of cellular functionality is improved by using these compounds as pharmacological tools to test the activities of ions-gated pores and electrophysiology due to their increased specificities and affinities to various components of numerous gated ion channels. Scorpion neurotoxins have three or four disulfide bridges that securely maintain their tridimensional backbone. There in vivo degradation was reduced by this characteristic, which naturally improved their effective binding duration and action. The development of new molecular engineering methods heavily influenced the creation of diverse peptide chimaera, and several recombinant scorpion peptides were produced. Another method to prevent bacterial growth is to modify the intracellular calcium signalling. Parabutoporin and opistoporins, isolated from Parabuthus schlechteri and Opistophthalmus carinatus scorpions, respectively, interact with linked G proteins as a result of this interaction to modify intracellular calcium signalling and exercise their antibacterial actions. These results suggest that these peptides have two distinct target locations: one is intracytoplasmic, suggesting contact with intracellular elements such DNA, RNA, and enzymes; the other has restricted effect on places on the outer membrane.

Homeostasis and Rheology

One of the toxicological consequences of scorpion venom is the change of hemodynamic and circulatory functions, which is mediated by either direct or indirect actions of neurotoxins. It's interesting to note that many blood and rheology injuries could benefit from the use of a few venomous substances. In Chinese ethnopharmacy, the use of scorpion venom to enhance blood rheology and homeostasis is the most striking. Surpassing therapeutic efficacy limitations caused by patient resistance and undesirable side effects is a typical hurdle in cardiovascular and thrombosis disorders. Since coagulation and its regulator factors have been found to be perturbed following scorpion stings, it is suggested that the entire scorpion venom or its components may have a role in regulating platelet aggregation. Utilizing renin-angiotensin system inhibition to control blood vasomotion is another alternative use for scorpion peptides in cardiovascular therapy. Hodgson and Isbister have examined the possible use of a number of venomous animal extracts in cardiovascular medication research as a result. They stated that a collection of peptides known as bradykinin potentiating peptides, which were recovered from various snakes and scorpions, prevent the breakdown of endogenous bradykinin and the synthesis of angiotensin II. The systemic blood pressure is lowered as a result of such effects. Furthermore, hypotensins from the venom of the Tityus serrulatus scorpion produced hypotension without interfering with the activity of the angiotensin converting enzymes. They provide a second strategy for the disease's wound healing because their mechanism of action is assumed to be mediated by nitric oxide release.

Immune diseases

The native Androctonus australis hemolymph and its partial fraction 1 (eluted by chromatography in G-200 Sephadex column at a maximum of 280-340 nm, with 0.01 molarity and an elution pH of 8.05) were found to stimulate the mitogenesis of human, rabbit, and mouse lymphocytes in in vitro studies, according to a 1980 publication by Brahmi and Cooper. Additionally, they did demonstrate that sugar derivatives can stop the erythrocytes' agglutination of lymphocytes after it has been activated. Tityus serrulatus gave its blessing to the improvement of immune cells' activity twenty years later. This leukocytosis was thought to be largely caused by a significant neutrophil release from the bone marrow to the blood vessel bed. The platelet-activating factor receptor signalling was a part of the mobilisation mechanism. Given that it appears that scorpion venom can alter the proliferative and/or functional characteristics of lymphoid cell lines. More recently, the ability of five distinct fractions from the venom of the aforementioned T. serrulatus, obtained by gel filtration chromatography, to alter immunological peritoneal macrophage secretions was evaluated. These subsequently made a difference in how macrophages functioned and may have interacted with one another in a beneficial way. One of these, an isolated -Ts toxin, achieves its immune regulating function through the production of pro- and anti-inflammatory molecules.

Neurological Diseases

Gated ion channel pore frameworks play a major role in controlling nervous system activity. These later ones control the movement of ions through the cell membrane and the firing and spread of action potentials, which are in charge of signal transmission. Any abnormal expression or function of pore components would lead to neurological disorders. Scorpion neurotoxins are regarded as a possible candidate for the development of neurological drugs due to their undeniably high specificity and affinity to diverse ions-gated channel components. The "magic" Buthus martensii Karschscorpion discussed in this article is frequently utilised in Chinese ethnomedicine to cure neurological conditions like apoplexy, epilepsy, and cerebral palsy. Recent research has shown that several of its elements have antinociceptive properties.

Discussion

Steadily for the past but not least, systems medicine techniques, where the main focus is on interactions of pathogenesis-influencing molecules that are typically active and/or dysregulated in various disease states, can also have a significant impact on the possibilities of uncovering novel disease networks. Research on miRNAs is a typical illustration of how systems medicine approaches are being used in this research context. It is not surprising that such miRNAs can be implicated in a number of clinical disorders, possibly simultaneously, given that miRNAs regulate transcripts, with one miRNA having the potential to downregulate the expression levels of up to hundreds of downstream target genes. The creation of bioinformatics web-tools like the miRNA BodyMap makes it possible to see more clearly the extent to which molecular interactions are directly controlled by miRNA members. Bengalensis heterometrus on ovariectomized female albino rats given methylprednisolone, scorpion venom has antiosteoporotic properties. The venom of the scorpion is believed to affect osteoclasts. The modification of the relevant regulatory variables appears to have accompanied

an increase in the bone mineral deposit (hormones, enzymes, and cytokines). A previous study found that the Kv1.3 scorpion toxin Kaliotoxin can inhibit the inflammatory bone resorption by blocking voltage-sensing potassium channels. These activities will probably help the bone resorption treatment work better.

Conclusion

There is systems medicine is changing the way academics, researchers, and clinicians approach medical research experiments. Greater understanding of the complicated and entangled, complex molecular interactions can be gained by simultaneously examining multilevel data from real experimental and computational in silico sources. Otherwise, the interactome would not be revealed because the connections between regulatory processes are not immediately apparent. This results in the discovery of novel dynamic interactions that are crucial for altering the course of medical disorders and, as a result, serve as clinically significant key molecules for the development of future diagnostic and therapeutic agents. Nevertheless, there are still significant obstacles to overcome because new technologies like next-generation sequencing and mass spectrometry (MS) generate enormous amounts of data, and the computational methodologies currently in use have only recently been able to handle sorting through such large amounts of data to find meaningful inferences for the posed research questions. Furthermore, there isn't a single tool that can be used to assist in the integration of multi-omics datasets, which leads to a high degree of subjectivity in the choice of the best systems-led techniques. Future systems medicine will also place more emphasis on molecular hubs, such as the several types of drug transporters found in cells, that have a significant and varied impact on the outcomes of polypharmacology therapy. The highly ambitious goal of creating the "virtual human," which would essentially encompass all the complex molecular networks and dynamic interactions on multiple omics-levels, should also be further implemented and harnessed. This would make it easier to develop drugs through multiple system perturbations with lead molecules due to the powerful computational elements offered by the "virtual Hu." The need for efficient systems medicine models that combine various data masses for accurate discovery of novel drug targets, therapies, and improved stratification of patient risk groups are further issues. This efficiency can only be attained by handling quantitative data correctly, using approved and standardised methodologies, and having efficient data transfer capabilities between various software programmes and data handling platforms in a seamless manner (as is the case with RDML when handling RT-qPCR data). Both the hemolymph and venom of scorpions contain a large variety of polypeptides that have a wide range of bioactivities and a high degree of selectivity for certain cell components. These polypeptides frequently have low molecular weights and are Disulfide Bridge stabilised in their compact form. Although more research is needed before starting any clinical applications, these assets suggest their potential usage as candidates for the creation of novel medications. Nevertheless, some peptides have advanced phase I trials. The toxicity and nonselective patterns for the adducted or diseased cells of scorpion compounds are two of their main barriers to clinical application. Such a strategy implies foresight in identifying the "wanted" scorpion and the material that is required. For instance, using animals from the Chactidae family would be unfair given the family's venoms' well-known lytic and cytotoxic effects when trying to isolate an anticancer cytotoxic peptide. Serial biochemical, pharmacological, and toxicological tests will isolate and define the necessary ingredient and enhance its efficacy and safety once the venom (or its derivative) satisfies the desired clinical objectives during the first round of bioassays. Goals will be adjusted as a result, and a decision will be made about whether to continue.

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Conflict of Interest

The author has no known conflicts of interested associated with this paper.

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