Identification of poisonous and non poisonous snake

INTRODUCTION

Snakes are one of the most interesting reptilian creatures of earth. They are interesting as for the purpose of study as well as research and that is so because of the one character they possess in them and that is there Poison which is called by the name of Venom. Unlike all reptile snakes are poisonous but not all of them. A few species among them failed to obtain that character. This venom act as both useful weapon as well as defense shield against its pray and enemy.

The snake venom is a hazardous protein and characterized by very complex compositions. It is slimy egg-like viscous liquid having slightly fishy smell. It is the complex set of harmful toxicants as well as proteins. Other than toxicants and proteins the snake venom contains several peptides, amino acids, carbohydrates, lipids, nucleosides, biological amines and metal ions, which make it even more complex than other normal proteins. Venom contains more than 20 kinds of enzymes and toxins, but the main ingredients of the venom are toxic proteins.

The toxic component present in snake venom varies according to the snake species or even the venom secreted by the same snake in different season may also vary. This changes the characteristic of different snake venom and decides its role in pharmacological, toxicological and medical field. Snake venom mainly consists of neurotoxins, cardiotoxins, toxins that cause blood clotting, bleeding toxins (that stops the blood clotting and blood remains to flow continuously even after injury), harmful enzymes and other major components. The cytotoxic venom is more effective than the neurotoxic type

venom, and it will work almost immediately to the prey such as the mouse and frogs.

Although the snakes are very calm and hideous animals (except a few ones) yet mortality rate associated with the snakebites is a serious public health problem in almost all the region of the world, especially in rural areas where medical facilities are low or absent. In India, majority of bites and mortality are due to King cobra, Naja naja, Daboia Russelli Russell's viper, Bangarus caeruleus (common krait) and Echis carinatus (saw-scaled viper).

[1. 1] Frequency of snake bite

About 35, 000 to 50, 000 people reportedly die of snake bite in India every year; however, the unreported cases may be more in rural India. Estimated snake bites and (death) cases were reported as 25, 000(30) in Europe; 6 20, 000(100) in Middle East; 45, 000(15) in USA and Canada; 3, 00, 000(5, 000) in Central and South America; 10, 00, 000(20, 000) in Africa; 40, 00, 000 (1, 00, 000) in Asia; 10, 000 (200) in Oceania all total worldwide 5 million (1, 25, 000). Death incidence due to snake bite is rather rare in Australia, Europe and North America but frequent in South Asia, South-East Asia and Sub-Sahar an Africa. In Zimbabwe on 274 cases studied, 4 out of 5 3, 6, 7 children died who are under 8 years old.

[1. 2] Identification of poisonous and non-poisonous snake

(source: www. buzzle. com/…/venomous-snake-identification-identifying-poisonous-snakes. html)

Poisonous snakes generally possess the characters like –

Vertically elliptical shaped cat like pupil.

A small depression (termed pit) between the eyes and nostrils.

Triangle shaped head e. g. Copperheads and rattle snakes, exception- Elapids.

Underside scales of tail go completely all the way across in a single row from the anal plate; the very tip of the tail may possess two scale rows.

Head and body both are seen during swimming time.

Generally of multiple colors. In contrast, non-poisonous snakes generally possess the characters like:

Round pupil in the center of eye.

U shaped head.

Two rows of scales from the vent to the tail end.

Only head is seen during swimming time.

Generally of one color.

Mostly stripes are from head to tail.

[1. 3] Utility of Snake Venom

Snake venoms are used to control heart diseases, high blood pressure, cancer (contortrostain produced by Agkistrodon contortrix- is cytostatic in nature and found to lower the growth rate of breast cancer in mice), tumor, polio, neurological disorders (enzymes from cobra venom were found to cure Parkinson s and Alzheimers diseases), excessive bleeding (a blood clotting

protein in Taipan venom stop bleeding during surgery or after major trauma), blood clotting (ancrod obtained from Malyan pit viper, used to develop angiotensin converting enzyme inhibitors to treat stroke victims), severe allergies amongst others. Other interesting areas of snake venom include the treatment of viruses (as venom contain phospholipidases which break down cell membrane), aging and some are even used in commercial wrinkle cream!

[1. 4] Phospholipase-A2

Phospholipase A2 is one of the most intensively studied membrane proteins which hydrolyze phospholipids at the sn-2 position to form fatty acid and lysophospholipid products. These are small proteins and the 3-D structures are known to high resolution for several species. Phospholipase A2 proteins are of high pharmaceutical concern since they are responsible for the release of arachidonic acid from membranes, and since the subsequent conversion of this fatty acid to leukotrienes and prostaglandins is part of the inflammatory response. The enzyme also shows very interesting interactions with the membrane on which it binds. It is activated in some way when it interacts with aggregated forms of the substrate, such as in micelles or in bilayers. Electrostatic and hydrophobic interactions are suspected to be involved in the binding of the enzyme to the membrane. Very little is known of the enzyme-membrane complex structure and why the enzyme reacts much more efficiently once it binds its substrates in an aggregated form.

The phospholipid molecule consists of a glycerol-3-phosphate (blue colour) esterified at its sn-1 and sn-2 positions to non-polar fatty acids (R1 and R2, respectively) and at its phosphoryl group to a polar head group, X.

Phospholipase A1 and phospholipase A2 cleave the acyl ester bonds at sn-1 and sn-2, respectively. Phospholipase C cleaves the glycerophosphate bond whereas phospholipase D removes the head group, X. PLA, phospholipase A; PLC, phospholipase C; PLD, phospholipase D.

Phospholipases2. png

Fig-1. 1: Phospholipase A2 Structure

[1. 5] Phospholipase-A2 (PLA2) Activity

After entering inside the body of human being venom containing PLA2 enzyme start affecting the cell membranes of almost all the cell organelles. Since cell organelles containing cell membrane are made up of phospholipids, hence this this phospholipids act as a reactant for phospholipase a2 and start reacting with it. This phospholipase a2 tends to form arachidonic acid which has an inflammatory sensation and this arachidonic acid further converted into PGG2 by using cyclooxygenases. This PGG2 further transcribed into PGH2 which forms 3 basic compounds PGD2, PGF2, and PGE2.

On the basis of the ester bond that is cleaved within a phospholipid molecule, phospholipases are grouped into four families, namely A, B, C and D. Phospholipase A enzymes cleave the acyl ester bond at either the sn-1 (phospholipase A1) or sn-2 (phospholipase A2) position (Figure 1). The Whoterm phospholipase B is given to phospholipases that hydrolyze acyl ester bonds at both sn-1 and sn-2 positions. Enzymes grouped under phospholipase C cleave the glycerophosphate bond, while phospholipase D enzymes remove the polar head group.

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Fig-1. 2: Activity Chain of Phospholipase A2 inside Cell Membrane

Phospholipase A2 is being suppressed by Lipocortins which is also known as Annexin. In human Annexin the common cellular protein is found inside the cell. However outside the cell the annexin is also found inside the blood because they are transported out of the cell into the blood. This is because of the lack of a signal peptide necessary for protein to be transported out of the cell.

Since there are different dataset had been already prepared but could not found the IC50 value, due to which the working on this dataset could not be carried out further.

[1. 6] Quantitative Structure Analysis Relationship (QSAR)

QSAR plays an important role in lead structure optimization and it can be predicted that QSAR method will become essential for handling the huge amount of data associated with combinatorial chemistry. 3D-QSAR has already been successfully applied to many data sets of enzyme and receptor ligands. The biological activity of molecules is usually measured in assays to establish the level of inhibition of particular signal transduction or metabolic pathways. Chemicals can also be biologically active by being toxic. Drug discovery often involves the use of QSAR to identify chemical structures that could have good inhibitory effects on specific targets and have low toxicity (non-specific activity). Of special interest is the prediction of Log P, which is an important measure used in identifying “ drug-likeness” according to Lipinski’s Rule of Five. While many Quantitative Structure Activity

Relationship analyses [9] involve the interactions of a family of molecules with an enzyme or receptor binding site, QSAR can also be used to study the interactions between the structural domains of proteins. As in the article Structural modeling extends QSAR analysis of antibody-lysozyme interactions to 3D-QSAR, protein-protein interactions can be quantitatively analyzed for structural variations resulted from site-directed mutagenesis. In this study, a wild-type antibody specific for lysozyme and 17 single and double mutants of the antibody were investigated. Quantitative models for the affinity of the antibody-antigen interaction were developed.

[1. 6. 1] 3D-QSAR

The 3D-QSAR methods have been developed to improve the prediction accuracies of 2D methods. 3D methods are computationally more complex and demanding than 2D approaches. In general, there are two families of 3D-QSAR methods: alignment-dependent methods and alignment-independent methods. Both families need experimentally or computationally derived bioactive conformations of ligands as templates for studies.

QSAR study revealed that alignment- independent descriptor and distance-based topology index are the most important descriptor in predicting apoptosis- inducing activity. 3D-QSAR study was performed using k-nearest neighbor molecular field analysis (kNN-MFA) approach for both electrostatic and steric fields. Three different kNN-MFA 3D- QSAR methods (SW-FB, SA, and GA) were used for the development of models and tested successfully for internal (q2> 0. 62) and external (predictive r2> 0. 52) validation criteria. Thus, 3D-

[1. 7] Objectives

To retrieve the three- dimensional coordinates of protein and known active molecules against phospholipase-A2.

To generate significant three-dimensional Quantitative Structure Activity Relationship model from active molecules.

To analyze protein-ligand interaction of known actives against phospholipase-A2 molecular docking studies.

To identify important scaffold of compound and their structural modification with helps in designing new molecules with improve activities.