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Evaluation of the antitumor effect of crude Cobra venom in mice with reference to clinicopathological changes.

Thesis Presented By

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Clinical Pathology

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Abstract

Snake venom is composed of different proteins and enzymes which have been shown to exert beneficial effects in treatment of certain diseases due to its various biological activities. The present study was divided into two experiments. Experiment one aimed to evaluate the clinicopathological effect of Naja haje snake venom at different doses on hematological, serum biochemical parameters, oxidative damage and histopathological alterations in mice. Results showed that administration of 2.1µg/ml venom caused anemia, leukopenia, hypoproteinemia, hypoalbuminemia, decreased A/G ratio and hepatic and renal GSH, while there were significant increases in the value of total and conjugated bilirubin, activities of ALT, AST and ALP, values of serum urea, creatinine and hepatic and renal MDA levels. Snake venom caused histopathological changes in the liver, kidney and spleen of mice. Experiment two was conducted to evaluate the antitumor effect of Naja haje snake venom by I/P injection of EAC tumor cells together with snake venom in different concentrations. Group of mice injected with tumor cells alone showed anemia, significant hypoproteinemia, hypoalbuminemia decreased A/G ratio, decrease of hepatic and renal GSH, increase of total leukocytic counts and platelet counts, values of total and conjugated bilirubin, activities of ALT, AST and ALP, values of serum urea, creatinine and hepatic and renal MDA levels. Values of the tested parameters were brought back to near normal levels in groups treated with different concentrations of snake venom.

Key words: Snake venom, Ehrlish ascitis carcinoma, Clinical pathology, Naja haje, Antitumor.

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Supervision Sheet

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Contents

List of Abbreviations

A.F.	Ascetic fluid
ANOVA	Analysis of Variance
a-ntx	long chain alpha neurotoxins
B.	Bothrops
BC	conjugated bilirubin
BU	unconjugated bilirubin
Bcl-2	B-cell lymphoma 2
BFV	Bungarus fasciatus venom
BjV	Bothrops jararaca venom
BthTX-I	myotoxin from Bothrops jararacussu snake venom
C.	Cerastes
Cdca	Crotalus durissus cascavella
Cdcol	Crotalus durissus collilineatus
Cdt	Crotalus durissus terrificus
Cdt	Crotalus durissus terrificus
CdtV	crotalus durissus terrificus snake venom
CN	Contortrostatin
CRiSPs	cysteine-rich secretory proteins
CTLs	C-type lectins
Cvv	Crotalus viridis viridis
D.	Daboia
DENV	dengue virus
EAC	Ehrlich Ascites Carcinoma
Ec	Echis coloratus
EMT	epithelial- mesenchym altransition
EPV	Echis pyramidum venom
FCA	Freund's complete adjuvant
Fig	figure
fl	Femtolitre
ft	Feet
g/dl	gram per deciliter
gp	group
H&E	Hematoxylin and Eosin stain
HIV	Human Immunodeficiency Virus
Hrs.	Hours
H-SN1	Hydrostatin-SN1
HSV	herpes simplex virus
I/P	Intra-peritoneal
I/V	Intravenous
I/M	intramuscular
IL-1β	interleukin 1beta
ILS%	Intermetiet Life Span
L.	Leishmania
LAAO	L-amino acid oxidase

mg/dl	milligram per deciliter
Mins.	Minutes
MjTX-II	myotoxic PLA2
MP	metallo proteases
MST	Mean Survival Time
N.	Naja
NT	Neurotoxin-Nna peptide
OVCAR-5	human epithelial carcinoma cell line of ovary cells
p.	Pseudechis
PLA2s	phospholipases A2
RAPD-PCR	Random Amplification of Polymorphic DNA- polymerase chain reaction
ROS	reactive oxygen species
RP- HPLC	Random Amplification High-performance liquid chromatography
S/C	Subcutaneous
SD	Standard deviation
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
SPSS	Statistical Package for Social Sciences
sv- cyst	snake venom containing cystatin a member of cysteine protease family inhibitors
SVMPs	snake venom metallo proteinases
SVT	snake venom toxin
TNF-α	tumor necrosis factor alpha
U.A.E	United Arab of Emirates
U/L	international unit
ul	microlitre
uM/g	micromoles per gram
VEGF	vascular endothelial growth factor
VSV	Vesicular Stomatitis Virus
WEV	Walterinessia aegyptia
Wt.	weigth
YFV	yellow fever virus

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1- INTRODUCTION

Venomous snakes are species of the suborder Serpentes that are capable of producing venom which is used by the snake for immobilizing prey via mechanical injection by fangs. Common venomous snakes include the families; Elapidae, Viperidae, Atractaspididae and some of the Colubridae **(McCartney et al., 2014)**. The Elapidae family of venomous snakes is found in tropical and subtropical regions around the world. It includes cobras, mambas, sea snakes and coral snakes. Several species of cobras are natives to Africa. The Egyptian cobra Najahaje found from southern Egypt to northern South Africa.

Snake venom is highly modified saliva made up of venom glands.The glands which secrete the zootoxins are a modification of the parotid salivary gland of other vertebrates and are usually situated on each side of the head below and behind the eye, encapsulated in a muscular sheath. The glands have large alveoli in which the synthesized venom is stored before being conveyed by a duct to the base of channeled or tubular fangs, through which it is ejected **(Hallidayand Tim, 2002).**

Venoms contain more than 20 different compounds, mostly proteins and polypeptides. It is a complex mixture of several substances, such as toxins, enzymes, growth factors, activators and inhibitors with a wide spectrum of biological activities **(Lipps, 1999).** These proteins are responsible for the toxic and lethal effect of the venom, enzymes play an important role in the digestion of prey, and various other substances are responsible for important but non-lethal biological effects. Some of the proteins in snake venom are very particular in their effects on various biological functions including blood coagulation, blood pressure regulation and transmission of the nervous or muscular impulse and have