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"Comparative studies on some adjuvants used in production of inactivated antirabies vaccines"

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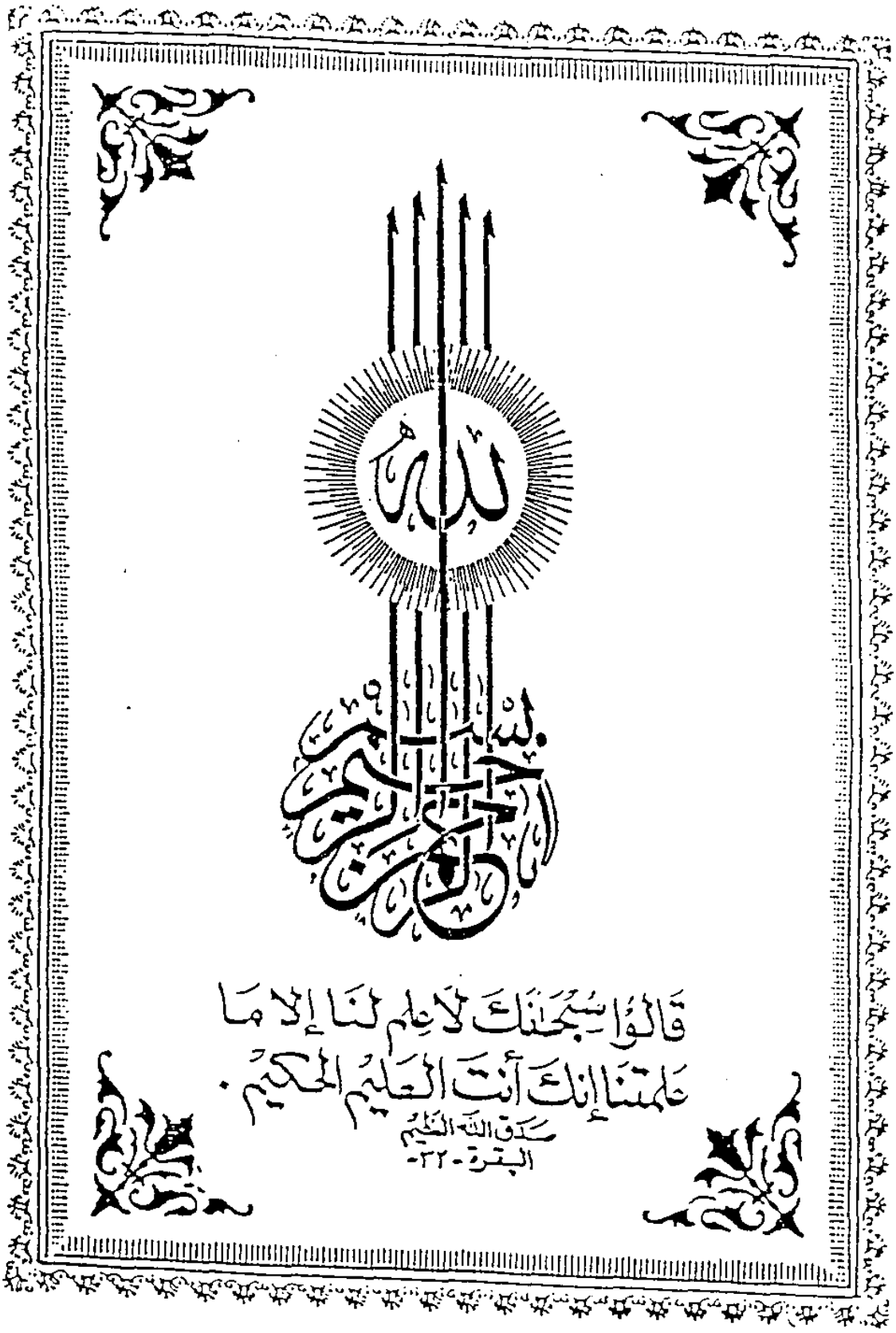

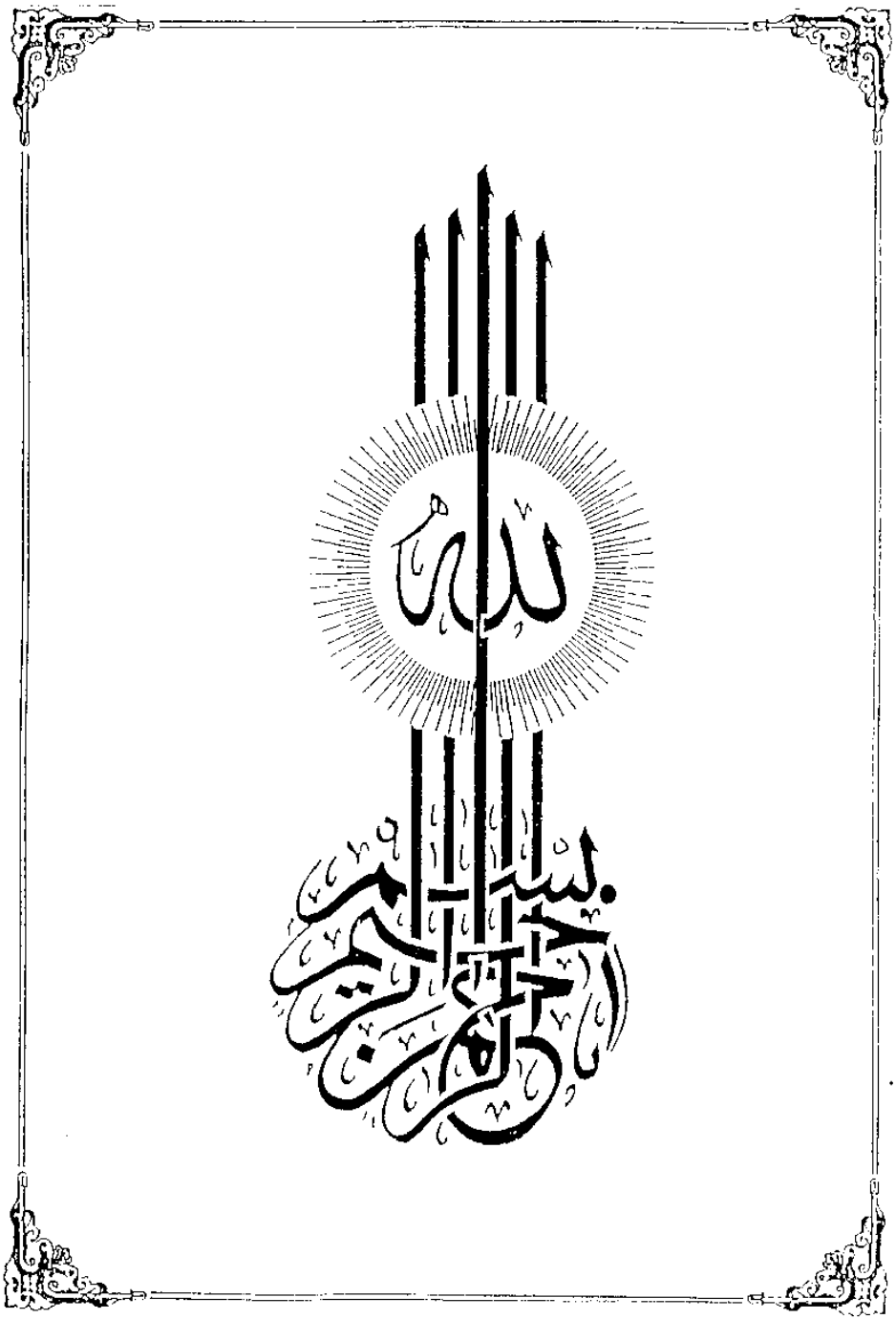

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APPROVAL SHEET

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LIST OF ABBREVIATIONS

AEI	==	Acetyl Ethyleneimine
BEI	==	Binary Ethyleamine
BHK	==	Baby Hamster Kidney Cell Line
BPL	==	Beta Propiolactone
CAV	==	Cell Associated Virus
CDC	==	Center Of Disease Control
CEO	==	Chicken Embryo
CFV	==	Cell Free Virus
CVS	==	Challenge Virus Strain
DEAD-D	==	Diethylaminoethyl -Dextrain
DEV	==	Duck Embryo Vaccine
DDW	==	Double Dist Water
ELISA	==	Enzyme Linked Immuno Sorbant Assay
FRV	==	Fixed Rabies Virus
HEP	==	High Egg Passage
HDCS	==	Human Diploid Cell Strain
HSA	==	Human Serum Albumin
IL-2	==	Interleukin- 2
LEP	==	Low Egg Passage
MLV	==	Modified Living Virus
NT	==	Nervous Tissue
NIH	==	National Institute Of Health
OPD	==	Orthophenyl Diamine
PBS	==	Phosphate Buffer Saline
RFFIT	==	Rapid Flurescent Focus Inhibition
RP	==	Relative Potency
SAD	==	Street Alabama Dufferine Strain
TC	==	Tissue Culture
VNT	==	Virus Neutralization Test
VNI	==	Virus Neutralization Index

INTRODUCTION

INTRODUCTION

Rabies is world wide , highly mortality disease affecting mammalian species . Rabies virus can infect all warm blooded animals and in nearly all instances , the infection ends in death .

It is caused by a virus belonging to the family Rabdoviridae and transmitted through abrasions and wounds contaminated with infected saliva of rabid animals.

The clinical features of rabies are similar in most species , but there is great variation between individuals .

The disease characterized by marked nervous excitement and irritability followed by loss of consciousness and ending with paralysis and death.

Rabies disease is a serious health problem in many parts of the world , in developing countries specially in Egypt , the authorities adopt a wide organized program for the control of canine rabies , such program is very important for a country such Egypt , which has an open desert without any natural boundaries separating it from other neighboring countries .

Since rabies is known to be an incurable disease , so vaccination is the powerful tool in combating the disease , the veterinary rabies vaccines are generally used for pre - exposure immunization of pet and farm animals .

Post - exposure treatment of animals is rarely applied as it is regarded as potentially too dangerous for man .

In human beings most of the vaccines are used in post - exposure therapy , pre-exposure immunization being reserved for the relatively little number of people who run some risk of infection because of their occupation .

Fermi , [1908] produced a vaccine consists of 5% aqueous goats or sheep brain suspension containing 0.5% phenol .

Koprowski and Cox , [1948] manufactured the chicken embryo vaccine by inoculating of day old chicken embryos intra-yolk sac with LEP virus strain and that type of vaccine is used successfully for pre exposure immunization of dogs only .

In 1955 , Peck modified the chicken embryo vaccine , by inoculating seven day old duck embryos free from salmonella , intra-yolk with a variant strain of PM at 12 - 13 th passage level , then the virus was inactivated with BPL to form the duck embryo vaccine .

Svet - Moldavsky , [1960] produced the suckling rat brain vaccine by i/c inoculation sukling rats (4 - 8 day old) with the original fixed virus of Pasteur strain , and inactivated by 1% phenol .

Ott and Heyke , [1962] suggested a vaccine in which the virus used is a tissue culture adapted strain by **Kissling [1958]** . The vaccine was used via i/m or s/c to dogs , cats , cattle , horses and sheep, "Hamster Kidney-CVS phenol inactivated vaccine" .

Fuenzalida , et. al. [1964] succeeded to obtain on a vaccine from suckling mice inoculated with special mice fixed rabies strain and inactivation is carried out by u/v .

Wiktor , et. al. [1964] prepared a vaccine for human by the inoculation of HDC-WI38 cell line with a seed virus lot prepared from PM strain and inactivated by BPL 1: 4000 for 18 hours at 4°c .

Abelseth , [1964] obtained on a vaccine from virus adapted on swine kidney cells after growing on the hamster kidney cells and chicken embryos.

Cabasso , et. al. [1965] prepared a vaccine from the LEP virus strain adapted to chicken embryo fibroblast cells . The vaccine was used as prophylactic for dogs only.

Brown , et. al. [1967] produced a vaccine by growing the HEP virus on a permanent dog kidney cell line .

Sikes and Larghi , [1967] produced a vaccine from suckling mice 3 - 4 days old were inoculated with 0.01% ml of fixed rabies virus, the virus was inactivated by BPL .

Kucera , et. al. , [1969] used the adapted tissue culture virus strain by **Kissling [1958]** and inactivated with formalin and used oil adjuvants , the vaccine was licensed for s/c use in dogs (2 ml) and cats (1 ml) .

In 1973 , Seligman produced a vaccine from rabbit , goat and sheep brains , it is consisted of suspension of 5% inactivated fixed rabies virus , containing 0.25% - 0.4% phenol and 1.0 % thiomersal .

Slimov and Morogova , [1973] produced a freeze - dried vaccine containing 5% sheep brain suspension of fixed rabies virus , 3.75% sucrose and not more than 0.25% phenol .

Lepine , et. al. [1973] prepared a freeze dried vaccine using the original Pasteur strain or PV_{11} strain , containing 75% sucrose and inactivated by BPL in 1: 4000 concentration .

WHO and Californial conference in 1979 recommended the prevention of using all alive vaccine to administrated for vaccination either in human beings or in veterinary use , due to reverse of the virulence of the vaccinated strains which may be happened , or due to incidence of focal infection in a clean area . So the using of inactivated vaccine is most safer , but in order to increase their potency , it must be combined with an adjuvant .

Adjuvant is a substance that , when used in combination within specific antigen , enhanced the levels of immmunity beyond those developed with the vaccines alone **(Roman , 1926)** .

It may act on a hapten or antigen enhancing its antigenic properties , or on the cells involved in the immune response , **(Jolles and Paraf , 1973)** .

The practical application of these substances has also widened from their classical use with vaccines , including tumour vaccines **(Bartlett and Kreider , 1981)** .