



**Cairo University**  
**Faculty of Veterinary Medicine**  
**Department of Virology**



# **Process Development of Nano-aluminum Hydroxide Adjuvanted Rift Valley Fever Virus Vaccine**

**A thesis submitted by**

**Shourok Essam Aly Abdel-Hady**

**(BVSc, Cairo University, 2012)**

**For the degree of Master of Veterinary Medical Sciences**

**(Virology)**

**Under Supervision of**

**Prof. Dr. Mohamed A. Shalaby**

Professor of Virology & Immunology  
Faculty of Veterinary Medicine  
Cairo University

**Prof. Dr. Ausama A. Yousif**

Professor of Virology  
Faculty of Veterinary Medicine  
Cairo University

**Prof. Dr. Karim El-Din Zaki**

Chief Researcher  
Veterinary Serum and Vaccine  
Research Institute

**2020**





**Cairo University**  
**Faculty of Veterinary Medicine**  
**Department of Virology**



## **SUPERVISION SHEET**

**Prof. Dr. Mohamed A. Shalaby**  
Professor of Virology & Immunology  
Faculty of Veterinary Medicine  
Cairo University

**Prof. Dr. Ausama A. Yousif**  
Professor of Virology  
Faculty of Veterinary Medicine  
Cairo University

**Prof. Dr. Karim El-Din Zaki**  
Chief Researcher  
Veterinary Serum and Vaccine  
Research Institute

**2020**





## Approval Sheet

This is to approve that Thesis presented by

**Shourok Essam Aly Abdel hady**

For the degree of MV.Sc. (Virology) has been approved by the  
examining committee

**Prof. Dr. Hanafy Mahmoud Madbouly**

Professor of Virology  
Faculty of Veterinary Medicine  
Bani sueif University

**Prof. Dr. Ahmed Abd El-Ghani El-Sanousi**

Professor of Virology  
Faculty of Veterinary Medicine,  
Cairo University

**Prof. Dr. Ausama Abd El-Raouf Abd El- Moneim Yousif**

Professor of Virology  
Faculty of Veterinary Medicine  
Cairo University (Supervisor)

**Prof. Dr- Mohamed Abd El-Hamid Shalaby**

Professor of Virology  
Faculty of Veterinary Medicine  
Cairo University (Supervisor)

2020



## *Dedication*

*To My Mother Sanaa El-Shihi the Most Wonderful and  
Heroic Mother ever*

*Essam Aly the Kindest and Most Patient Father*

*My Sweet and Gorgeous Sister Toka Aly*

*My Great and Loving Brother Mostafa Aly*

*To Every member of My Big Family*

*The Soul of My Grand Parents*

*To my friends who become family*

*Soad Eid El-Sayed*

*Hadeer Moustafa*

*Ahmed El-Wakeel*

*Mahmoud El-Gamal*

*Ahmed Ibrahim*

*Dina Tarek*





## **Acknowledgment**

*First and Foremost, I am deeply grateful to **ALLAH**, the most Merciful and the Most Beneficent for unlimited and continuous blessings on me.*

*I would like to express my sincere gratitude to **Prof. Dr. Mohamed A. Shalaby** for his efforts and continuous support not only as a supervisor but also as one of the most positive and helpful persons who greatly contributed to the veterinary medicine in Egypt and continues to be a great role model to us as for being a symbol of dedication, respect and hard work.*

*I am extremely grateful to **Prof. Dr. Ausama Yousif** as this thesis couldn't be completed without his bright ideas, enthusiasm, precise and insightful comments and I am mostly thankful for him for permanently changing my mind set with his teaching techniques that gave me the chance to experience the joy of curiosity and free thinking and translating the ideas to reality, I no longer perceive the world as I used to and that's something I will be forever thankful for.*

*I am thankful to all members of the Rift Valley Fever department at VSVRI for their help and support, specially **Dr. Karim El-Din Zaki** for his constant trust, support and motivation throughout the whole period he served as the head of the department.*

*My sincere thanks to **Dr. Noha Ezz El-Din** for her great assistance, her patience kindness and massive support and for being a helpful colleague and a great friend and sister.*

*My appreciation also extends to my colleagues at VSVRI who were greatly helpful and shared their knowledge and experiences with me **Dr. Walaa Abd Elmoneim** and **Dr. Marwa Yehia**.*

*I am indebted to **Dr. Neama Arif** at Cairo's Veterinary Medicine Directorate for her great support, encouragement, help and for being a wonderful woman and a thoughtful and caring director, also thanks to **Hend Hassan** and **Dina Magdi**.*

*I am grateful for having a great team of devoted, loving and hardworking colleagues namely **Soad Eid**, **Hadeer Moustafa**, **Mahmoud El-Gaml** and **Ahmed El-Wakeel**.*

*Thanks to **Mohamed Gaber Kotb** and **Wessam Ahmed Tawfik**,*





**Cairo University**  
**Faculty of Veterinary Medicine**  
**Department of Virology**



**Name:** Shourok Essam Aly.

**Nationality:** Egyptian.

**Date of Birth:** 27/05/1990.

**Place of Birth:** Cairo.

**Specification:** Virology.

**Thesis Title:** Process Development of Nano-aluminum Hydroxide  
Adjuvanted Rift Valley Fever virus vaccine.

**Abstract**

In this study the aluminum hydroxide adjuvant gel used widely in a lot of human and animal vaccines and currently solely used as an adjuvant in the locally produced inactivated Rift Valley Fever vaccine was treated by ultrasonication in the presence of trehalose for dispersion of its particles. The dispersed aluminum hydroxide adjuvant was extensively studied where various physical characters were determined. The particle size of aluminum hydroxide was significantly reduced as the aggregates size ranging from 1-20  $\mu\text{m}$ . As a result of dispersion, the TEM image of vaccine showed a change of the content from nonuniform and large aggregates of aluminum hydroxide with Rift Valley fever inactivated virus diffused in it to uniform particles with aluminum hydroxide adsorbed on virus surface and having a diameter of 300 nm. The vaccine with dispersed aluminum hydroxide was used in immunizing mice and showed superiority in immunogenicity when compared to the conventional vaccine.

**Keywords**

RVF, Nano, Aluminum hydroxide, ultrasonication



## LIST OF CONTENTS

<b>Title</b>	<b>Page No.</b>
<b>Chapter (1):</b> Introduction	<b>1</b>
<b>Chapter (2):</b> Review of literature	<b>4</b>
<b>Chapter (3):</b> Published research paper	<b>42</b>
<b>Chapter (4):</b> Discussion	<b>57</b>
<b>Chapter (5):</b> Conclusion and recommendation	<b>67</b>
<b>Chapter (6):</b> English Summary	<b>70</b>
<b>Chapter (7):</b> References	<b>72</b>
<b>Chapter (8):</b> الملخص العربي	<b>١</b>



**LIST OF TABLES**

<b>Table No.</b>	<b>Title</b>	<b>Page No.</b>
1	RVFV host range and disease severity	7
<b>TABLES ON PUBLISHED PAPER</b>		
1	Adsorbed protein values	51
2	Neutralizing index log mean values and challenge results	52