



# **Effect of Moderate Intensity Noise Exposure on the Cochlea of Adult Male Guinea Pig and the Possible Protective Role of Pravastatin: Histological and Immunohistochemical Study**

*Thesis*

*Submitted for Partial Fulfillment of Master Degree in  
Histology and Cell Biology*

Presented by

**Hend Farid El-said Ismail**

***M.B, B.Ch.***

***Demonstrator of Histology and Cell Biology  
Faculty of Medicine, Ain Shams University***

Under Supervision of

**Dr. Suzi Hanafy Ibrahim**

Professor of Histology and Cell Biology  
Faculty of Medicine, Ain Shams University

**Dr. Hany Kamal Kamel Mostafa**

Assistant Professor of Histology and Cell Biology  
Faculty of Medicine, Ain Shams University

**Dr. Azza Abd El Moneim Attia**

Assistant Professor of Histology and Cell Biology  
Faculty of Medicine, Ain Shams University

Faculty of Medicine  
Ain Shams University

**2017**

## Acknowledgment

Thanks first and last to **ALLAH** for guidance, support and care in every step in our lives.

I have the greatest pleasure to express my deepest gratitude to **Prof. Dr. Suzi Hanafy Ibrahim**, Professor of Histology and Cell Biology, Faculty of Medicine, Ain Shams University, for suggesting the thesis theme, plan of work, and for her continuous encouragement, supervision and support so that this work has been accomplished.

I wish to express my appreciation to **Dr. Hany Kamal Kamel Mustafa**, Assistant Professor of Histology and Cell Biology, Faculty of Medicine, Ain Shams University, for his support, great assistance and helpful discussions throughout the present work. His skillful scientific guidance during various steps of the work helped to achieve this work.

Also, I want to express my appreciation to **Dr. Azza Abd El-Moneim Attia**, Assistant Professor of Histology and Cell Biology, Faculty of Medicine, Ain Shams University, for her guidance and help in the field of practical laboratory work. Her close supervision helped me to complete this work.

My greatest thanks and best regards to all **my professors and my colleagues** in the department of Histology and Cell Biology, for their cooperation and valuable advices.

Lastly, I found no words to express my appreciation, gratefulness, love to all members of **my family**, without their support, encouragement and help this work would have not been fulfilled.

# List of Contents

	Page No.
List of Diagrams.....	i
List of Histograms.....	ii
List of Tables.....	iii
List of Abbreviations.....	iv
Abstract.....	1
Introduction and Aim of the Work.....	3
Review of Literature:	
▪ Noise Pollution.....	6
▪ Normal Cochlear Structure.....	15
▪ Statins.....	24
Materials and methods.....	30
Results.....	43
Discussion.....	156
Summary and Conclusion.....	168
Recommendations.....	174
References.....	175
Arabic Summary	

## List of Diagrams

<b>Diagram No.</b>	<b>Title</b>	<b>Page No.</b>
<b>Diagram I</b>	Diagram of the cochlear canal	<b>18</b>

## List of Histograms

<b>Histogram No.</b>	<b>Title</b>	<b>Page No.</b>
<b>Histogram I</b>	Noise levels for the main squares of greater Cairo governorate	<b>10</b>
<b>Histogram II</b>	Noise levels for commercial and administrative areas of Cairo governorate	<b>11</b>
<b>Histogram III</b>	Noise levels in areas located on main roads of Cairo governorate	<b>12</b>
<b>Histogram IV</b>	Mean surface area of spiral ganglion in neurons in different group.	<b>149</b>
<b>Histogram V</b>	Mean area percentage of Nissl's granules in spiral ganglion neurons in different groups.	<b>151</b>
<b>Histogram VI</b>	Mean area percentage of melanin in stria vascularis in different groups.	<b>153</b>
<b>Histogram VII</b>	Mean number of Caspase 3 positive neurons in spiral ganglion/HPF in different groups.	<b>155</b>

## **List of Tables**

<b>Table No.</b>	<b>Title</b>	<b>Page No.</b>
<b>Table I</b>	The mean surface area of spiral ganglion neurons of different groups.	<b>148</b>
<b>Table II</b>	The mean area percentage of Nissl's granules in the spiral ganglion neurons of different groups.	<b>150</b>
<b>Table III</b>	The mean area percentage of melanin in stria vascularis of different groups.	<b>152</b>
<b>Table IV</b>	The mean number of Caspase 3 positive neurons in spiral ganglia/HPF of different groups.	<b>154</b>

## List of Abbreviations

<b>dB</b>	Decibels
<b>EDTA</b>	Ethylene diamine tetra acetic acid
<b>GSH</b>	Glutathion
<b>HCs</b>	Hair cells
<b>H&amp;E</b>	Hematoxylin and Eosin stain
<b>HMG-CoA</b>	3-hydroxy-3-methyl-glutaryl-CoA
<b>4-HNE</b>	4- hydroxynonenal
<b>IHCs</b>	Inner hair cells
<b>IL6</b>	Interleukin 6
<b>LDL</b>	Low-density lipoprotein
<b>LSD</b>	Least significance difference
<b>NIHL</b>	Noise-induced hearing loss
<b>NS</b>	Non-significant
<b>OHCs</b>	Outer hair cells
<b>PBS</b>	Phosphate buffered saline
<b>ROS</b>	Reactive oxygen species
<b>S</b>	Significant
<b>SEM</b>	Scanning electron microscope
<b>SMA</b>	Spiral modular artery

<b>TEM</b>	Transmission electron microscope
<b>TNF<math>\alpha</math></b>	Tumor necrosis factor $\alpha$
<b><math>\mu\text{m}</math></b>	Micrometer
<b>WHO</b>	World health organization

# ***Abstract***

-

**Background and aim of the study:** Noise-induced hearing loss (NIHL), which is the second most common type of sensorineural hearing loss after presbycusis, is an irreversible disorder but potentially preventable. Noise induced hearing loss is a major health problem, because opportunities for overexposure abound, and exposures that damage hearing are not necessarily painful or even annoying. Extensive studies have documented the damaging effects of high-intensity acoustic overexposures on the cochlea, but only few works have focused on the danger of over exposure to moderate noise levels on the cochlea. Statins have recently been proposed to prevent NIHL so, this study was conducted to evaluate the effects of moderate intensity noise overexposure on the histological structure of the cochlea and to evaluate the possible protective role of Pravastatin.

**Materials and Methods:** Thirty adult male guinea pigs were included in the present study. Animals were divided into three groups: Group I (control group) (12 animals), Group II: 12 guinea pigs were further subdivided into two equal subgroups. Subgroup IIa animals were exposed to noise 70-90 decibels (dB) for 6hr/day for 6 weeks then sacrificed. Subgroup IIb were exposed to noise and given Pravastatin once daily for 6 weeks from the 1st day of exposure to noise then sacrificed. Group III: recovery group (6 animals) were exposed to noise for 6 weeks then were left for spontaneous recovery for 4 weeks. The cochleae were dissected, decalcified and processed for histological and immune-histochemical study.

**Results:** Light and scanning electron microscopic examination of the cochleae revealed that noise exposure resulted in various degrees of damage of hair cells and their stereocilia, stria vascularis, cochlear nerve fibers and spiral ganglia. The spiral ganglia neurons showed increased

expression of Caspase 3. Administration of Pravastatin resulted in improvement of the structure of the cochlea compared to the exposed and the recovery groups. These results were confirmed by the morphometric and statistical results.

**Conclusion:** Exposure of guinea pigs to moderate intensity noise have irreversible damaging effects on the cochlear structure and concomitant administration of Pravastatin daily showed protective effects on these damaging effects.

Keywords: Noise induced hearing loss, Pravastatin, presbycusis, Caspase 3.

# ***Introduction***

-

## **Introduction**

Environmental pollution becomes more severe and widespread due to population growth, urbanization and industrialization in the cities (**Ozdemir et al., 2014**). Migration of people from rural to urban areas, expansion of cities and infrastructure development are important factors resulting in motorization and consequent increase in levels of various urban pollution (**Mishra et al., 2010**).

There are many factors which cause the environmental pollution and one of those undesired and unpleasant factors is ‘noise’ which affects the quality of life (**Haq et al., 2014**). Many people are exposed to potentially hazardous noise levels in their daily modern life, such as noise from work environments, urban traffic and household appliances (**Rafi et al., 2014**). Environmental noises cause stress and have direct consequences on the psychological and physiological health (**Hosseini and Sabahi et al., 2014**).

Noise leads to many health effects among which noise induced hearing loss (NIHL) is the most common (**Jahani et al., 2016**). It is one of the most important consequences of exposure to noise in both developed and developing countries (**Fausti et al., 2005**).

Noise induced hearing loss is a major health problem, not only because of the abounding opportunities for overexposure but also because potentially damaging exposures are not necessarily painful or even annoying (**Ivory et al., 2014**).

The harmfulness of noise to hearing depends on the sound level, the duration of exposure, and the sensitivity of the exposed person or animal (**Basner et al., 2014**).

Damaging effects on the cochlea of high-intensity acoustic overexposures have been extensively documented, but only few works have focused on the danger of moderate noise levels (**Gannouni et al., 2015**).

Although some methods have been studied for treatment and prevention of NIHL, there is still no acceptable treatment for the disease (**Oishi and Schacht, 2011**).

Different kinds of statins are currently used as cholesterol-lowering agents, though they have other powerful pleiotropic effects on the body independent of this effect (**Jahani et al., 2016**). Recently, statins have attracted even more attention due to their antioxidant, anti-inflammatory, anti-ischemic, and blood-brain barrier repairing effects (**Ersoy et al., 2014**).

## ***Aim of the Work***

-