
" قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَاإِلاَّ مَا
عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيم"

صدق الله العظيم

سورة البقرة

آية ٣٢

# ULTRASTRUCTURAL AND IMMUNOHISTCHEMICAL STUDY ON THE EFFECT OF CERTAIN WIDELY USED ANTIDEPRESSANTS ON SUBMANDIBULAR SALIVARY GLAND OF RATS

**Thesis**

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*My Dear Mother*

*My Kind Husband*

*My Lovely Daughters*

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**ABSTRACT**

Amitriptyline is one of several tricyclic antidepressants used for treatment of depression. Mirtazapine is a tetracyclic piperazino azepine, which had a different structure from any other currently used antidepressants with fewer side effects. This study was designed to investigate the effects of amitriptyline and mirtazapine antidepressants on the submandibular salivary glands of the rats. A total of 100 male albino rats were used and divided into 5 groups (20 rats each). Group I was control group, group II was given a daily single therapeutic oral dose of amitriptyline for 8 weeks and group III was given a daily double oral dose of amitriptyline for the same period. Group IV was given a daily single oral therapeutic dose of mirtazapine for 8 weeks and group V was given a daily double oral dose of mirtazapine for the same period. Histological examination of submandibular salivary glands revealed degenerative changes and stagnation of secretion in the groups of both drugs .These degenerative changes increased from single to double dose of the drug. There was a highly significant difference of the mean value for optical density of S-100 protein between all groups.

**Keywords**: antidepressants; salivary glands; amitriptyline; histological structure; mirtazapine; depression, S-100 protein.

## الملخص

الأميتريبتيلين هو واحد من عدة مضادات الاكتئاب الثلاثية الحلقات ويستخدم في علاج الاكتئاب. الميرتازابين وهو رباعي الحلقات وله بنية مختلفة عن مضادات الاكتئاب الآخرى المستخدمة حاليا ويتميز بقلة المضاعفات الجانبية. والهدف من هذه الدراسة هو تقصي أثر الأميتريبتيلين و الميرتازابين على الغدد اللعابية تحت الفكية للفئران. واستخدم ١٠٠ من فئران التجارب البالغين الذكور وقسمت إلى ٥ مجموعات (٢٠ فأر لكل مجموعة). المجموعة الأولى واستخدمت كضوابط والثانية أعطيت جرعة يومية مكافئة للجرعة العلاجية من الأميتريبتيلين عن طريق الفم لمدة ٨ أسابيع. والمجموعة الثالثة أعطيت جرعة يومية مكافئة لمضاعفة الجرعة العلاجية من الأميتريبتيلين لنفس الفترة. أما المجموعة الرابعة فقد أعطيت جرعة يومية مكافئة للجرعة العلاجية للميرتازابين عن طريق الفم لمدة ٨ أسابيع. والمجموعة الخامسة وقد أعطيت جرعة يومية مكافئة لمضاعفة الجرعة العلاجية من الميرتازابين لنفس الفترة. وقد أظهر الفحص الهيستولوجي والالكتروني للغدد العلاجية تحت الفكية تغيرات وتراكم الإفرازات في مجموعات العقارين. وهذه التغيرات ازدادت من جرعة واحدة إلى جرعة مضاعفة وكان هناك اختلاف كبير في متوسط الكثافة البصرية لبروتين اس ١٠٠ بين كل المجموعات.

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# *Introduction*

# INTRODUCTION

Depression is a major public health problem, which is predicted to be the second disease after cardiovascular problems that leading to disability all over the world by 2020. It affected the total health status and patients with depression generally experience worse outcomes. Depression is wide spread among women and in most countries; the prevalence is twice that among men of the same age ***(Murray and Lopez, 1990).***

Depression is mental illness in which a person experience deep sadness and diminished interest in nearly all activities. Sever depression also called major depression which can dramatically impair a person's ability of function in social situation and at work. People with major depression often have feelings of hopelessness and worthlessness as well as thoughts of committing suicide. Anyone, regardless of age, gender, race, or socioeconomic status, can suffer from depression ***(Harrington et al., 1990).***

In addition the specific complaints of headache, back pain, abdominal pain, joint pain and chest pain were frequently endorsed by depressed patient in primary care setting. The common occurrence of depression and pain symptoms was the main reason that depression was frequently unrecognized and therefore untreated in primary care. The somatic symptoms predominated and might distract attention from typical

depressive symptoms ***(Kroenke et al., 1994).*** The new emphasis on pain as the "fifth vital sign" by both Joint Commission on Accreditation of Health Care Organization and the Veterans Health Administration provided an opportunity for better reorganization and understanding the interaction between depression and pain. ***Katon and ciechanowski (2002)*** also reported that, depression was under recognition but poorly treated by primary care physicians and specialists. Numerous studies in developed countries reported that only half of the patients with depression in primary care or general hospital setting were identified and even fewer were adequately treated. ***Rugulies (2002) and Keefe et al., (2002)*** found that there was an association between arthritis, cardiovascular disease and depression. Also they found that, the high rates of poorly treated depression were the leading factor to high rates of suicide among medical subspecialty clinic depressed patients.

***Stewart et al., (2004)*** stated that depression rates were slightly higher in the United States and slightly lower in Europe but followed the same sex based pattern. In addition to personal suffering, depression had a detrimental effect in general health, family well being, work productivity and health care costs. It might also lead to self injury and suicide.

It had been known for many years that treatment of depression was carried out using antidepressants. From these antidepressants, firstly discovered was tricyclic antidepressant.

. ***Haller et al., (2007)*** reported that tricyclic antidepressants (e.g. amitriptyline) were commonly employed orally to treat major depressive disorders. Tricyclic antidepressants had been shown to be of substantial benefit in various chronic pain condition associated with depression. In addition ***Kim et al., (2008)*** reported that mirtazapine was a newer and effective medication for treatment of depression. They also found that mirtazapine improved nausea, sleep disturbance, pain and quality of life.

Treatment of depression with antidepressant had many side effects as dizziness, insomnia, fatigue, xerostomia and constipation so that, attention had been directed towards studies of the side effects of the antidepressant drugs used and their potential hazards.