Mona maghraby

بسم اللّه الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني

Mona maghraby

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

Mona maghraby

بعض الوثائق الأصلية تالفة
وبالرسالة صفحات لم ترد بالأصل

ULTRASTRUCTURAL INVESTIGATION ON THE EFFECT OF SILDENAFIL CITRATE ON THE GINGIVA AND SUBMAXILLARY SALIVARY GLAND OF THE RAT

A

Thesis

Submitted in partial fulfillment for master degree in oral biology

By

Radwa Hamed Mohamed Hegazy

B.D.S

Faculty of Oral and Dental Medicine

Cairo University

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بسم الله الرحمن الرحيم

"قالوا سبحانك لا علم لنا الا ما
علمتنا انك انت العليم الحكيم "

"صدق الله العظيم"

سورة البقرة اية (٣٢)

Supervisors

Prof. Dr. Laila Sadek Ghali

Head of the Oral biology department

Faculty of Oral and Dental Medicine

Cairo University

And

Dr. Manal Safwat El-Assaly

Associate Professor

Oral Biology Department

Faculty of Oral and Dental Medicine

Cairo University

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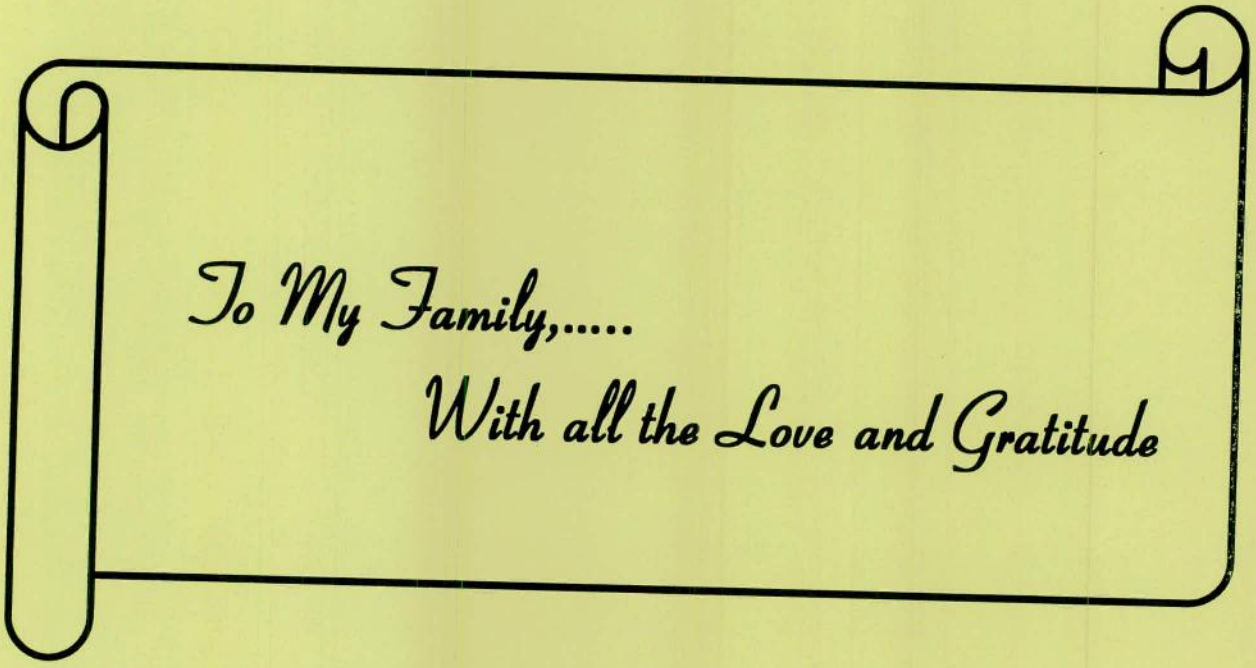
To My Family,.....
With all the Love and Gratitude

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INTRODUCTION

INTRODUCTION

Sildenafil, A selective cyclic guanosine monophoshate dependent phosphodiesterase type 5 inhibitor, induces vasodilatation by enhancing the smooth muscle relaxant effects of nitric oxide ***(Glossmann et al., 1998 & Moreland et al., 1998).*** The enhanced dilatation of blood vessels and lacunar spaces in the corpus covernosum leads to improved penile erection in patients with erectile dysfunction ***(Boolell et al., 1996).*** Sildenafil was originally developed first for treatment of cardiac ischemic condition because of its vasodilatory effect. ***(Jackson et al., 1999)***

Sildenafil citrate (Viagra), an oral medication for the treatment of erectile dysfunction does not cause erection by itself but potentiates the effect of sexual stimulation on the vascular channels of the corpus covernosum. Although the drug is marketed solely as therapy for impotence, its ability to intensify and prolong the erectile responses has led to its use as a sexual potency drug ***(Marmor & Kessler 1999).***

An extensive population based survey, confirmed that erectile dysfunction affects millions of men allover the world & reported that the age associated prevalence rates is 39% at 40 years of age and 67% at 70 years old men. ***(Isidori et al., 1999)***

Greiner & Weigel (1996) reported that erectile dysfunction is a multifactorial disease due to organic and/or psychological factors. Although non fatal, it adversely affects the quality of life resulting in depression, anxiety and poor self esteem.

Because erectile dysfunction represents a major clinical problem, many surgical and medical lines of treatment were tried including

vacuum devices, prosthetic implants and vasoactive drugs that are locally injected into the corpus cavernosum or inserted into the urethra. However each of these measures were unsatisfactory ***(Droller et al., 1993 & Licht 1998).***

The physiologic mechanism of erection involves release of nitric oxide (NO) in the corpus covernosum from endothelial cells. NO then activates the enzyme guanylate cyclase which results in increased levels of cyclic guanosine mono-phosphate (cGMP) producing smooth muscle relaxation and allowing inflow of blood ***(Goldstein et al., 1998).***

In the presence of Sildenafil, cGMP is quickly degraded by phosphodiesterase type 5(PDE5) a predominent isoenzyme in the corpus covernosum converting cGMP to guanosine mono-phosphate (GMP). In the presence of Sildenafil which is a potent and selective inhibitor of PDE5, the NO-cGMP mediated relaxation pathway remains activated ***(Boolell et al., 1996).***

Invitro studies have shown that Sildenafil has an effect not only on PDE5 but also on other known phosphodiesterases, however its effect is more potent on PDE5 which is also involved in cardiac contractility. PDE6 an enzyme found in the retina is also affected by Sildenafil giving the basis for abnormalities in vision observed with high doses.

In addition to human corpus cavernosum smooth muscles, PDE5 is also found in other tissues including platelets, vascular & visceral smooth muscles and skeletal muscles. The inhibition of PDE5 in these tissues by Sildenafil may be the bases for the enhanced platelet anti-aggregatory activity of NO observed invitro, inhibition of platelet thrombus formation invivo and peripheral arterial-venous dilatation invivo ***(Pfizer Inc. 1998).***

It has been reported that Sildenafil, nitroglycerines and other NO donors resulted in decrease in systemic vascular resistance and blood pressure in healthy humans ***(Das & Kumar 1995 & Stamler et al., 1994)***. Thus Sildenafil is contraindicated absolutely in patients receiving nitrate therapy because of the potential for significant hypotensive effect and vasodilator symptoms such as light headedness, headache and nausea ***(Kloner & Zusman 1999).*** Moreover ***Gibaldi (1999)*** reported many records of sudden death & post marketing side effects between the users of Sildenafil most of them are related to vasodilatation as flushing, nasal congestion, intestinal disturbances, abnormal vision & digestive adverse effects like vomiting, nausea, glossitis, gastritis, dry mouth & rectal hemorrahge.

In spite of that ***Kloner and Jarow (1999)*** reported that Viagra is a quite safe drug, well tolerated by most patients without serious effects even in cardiac patients.