

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا

عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ

الْحَكِيمُ"

سورة البقرة ٣٢

**P-Cadherin Expression in Oral Mucosa
of Smoker Patients.**

(An Immunohistochemical Study)

Thesis

*Submitted to Oral Medicine and Periodontology Department, in
partial fulfillment of the requirements for the
Master Degree*

In

Oral Medicine, Oral Diagnosis and Periodontology

By

Sherien Ali Hassan

B.CH.D.

Oral Medicine, Oral Diagnosis and Periodontology Department
(Cairo University)

Faculty of Oral and Dental Medicine
Cairo University

2009

Supervisors

Professor Dr. Soheir Mohamed Gaafar

Professor of Oral Medicine, Oral Diagnosis and Periodontology

Faculty of Oral and Dental Medicine

Cairo University

Dr. Hossam El-Din Hussein

Associate professor of General Pathology

Faculty of Medicine

Cairo University

Dr. Shaheenaz Gamal El-Din El-Ashery

Lecturer of Oral Medicine, Oral Diagnosis and Periodontology

Faculty of Oral and Dental Medicine

Cairo University

Acknowledgment

First and foremost, I would like to express my greatest thankfulness to *ALLAH*, who created man and gave him the knowledge to think, believe and worship.

I would like to express my sincere gratitude and appreciation to professor Dr. Soheir Gaafar, professor of Oral Medicine, Oral Diagnosis and Periodontology Department, Faculty of Oral and Dental Medicine, Cairo University. I will remain grateful for her valuable guidance, continuous scientific supervision, spiritual encouragement, unforgettable efforts and proper planning that lead to the formation of this work.

Special thanks to Dr. Hossam El-Din Hussein, associate professor of General Pathology Department, Faculty of Medicine, Cairo University; for his great effort and endless help without whom this work would not have been possible.

My great thanks to Dr. Shaheenaz Gamal El-Din El-Esheiry, lecturer of Oral Medicine, Oral Diagnosis and Periodontology Department, Faculty of Oral and Dental Medicine, Cairo University; for her close supervision, her meticulous observation and for giving me generously of her time. I will remain grateful for her guidance that helped me all through this work.

Most sincere thanks to all members in Oral Medicine, Oral Diagnosis and Periodontology Department, Cairo University; for their continuous encouragement and support.

Dedication

This work is especially dedicated to my family,

My dear lovable parents,

My dear brother,

*Who gave me love, care and support
throughout my life.*

List of figures

No	Heading	Page No
1	Schematic overview of the classical CD (P-, E- and N-) depicting representative molecules for the respective subfamilies (<i>Angst et al., 2001</i>).	13
2	Classical CD-mediated cell-cell adhesion: classical CDs form lateral homodimers, which interact with homodimers of the neighbouring cell through CD repeat 1 (<i>Angst et al., 2001</i>).	13
3	Steps in the development of invasive SCC: Invasive SCC is preceded by premalignant (benign keratosis and mucosal dysplasia) and pre-invasive (carcinoma-in-situ) lesions. The role of benign keratosis is less certain (<i>Crawford, 2008</i>).	37
4	Clinical photograph for a patient with smoker's keratosis (45 y old male) showing a white patch on the left buccal mucosa.	42
5	Clinical photograph for a patient with smoker's keratosis (40 y old male) showing multiple white patches on the right buccal mucosa.	42
6	Histogram showing mean optical density for normal tissues (control group) and smokers not suffering from smoker's keratosis (group II).	56
7	Histogram showing mean optical density for normal tissues (control group) and smokers suffering from smoker's keratosis (group III).	57

8	Histogram showing mean optical density for group II and group III.	59
9	Histogram showing mean optical density for the three studied groups.	61
10	Histogram showing mean area % for the control group and group II.	63
11	Histogram showing mean area % for the control group and group III.	64
12	Histogram showing mean area % for group II and group III.	66
13	Histogram showing mean area % for the three studied groups.	68
14	Histogram showing correlation between mean optical density and mean area % in group II.	70
15	Photomicrograph of normal epithelium of buccal mucosa section (group I) showing the normal stratification of the stratified squamous epithelium and normal underlying connective tissue (H&E, X100).	72
16	Photomicrograph showing immunostaining for P-CD in the basal and parabasal cells only (DAB, X200).	72
17	Photomicrograph showing positive reaction of P-CD in both basal and parabasal cell layers only masked by blue binary color to evaluate area % (X400).	73
18	Photomicrograph showing positive reaction of P-CD in both basal and parabasal cell layers only masked by red binary color to evaluate optical density (X400).	73
19	Photomicrograph of hyperplastic stratified squamous	75

	epithelium of buccal mucosa section (group II) showing acanthosis and parakeratin layer (H&E, X40).	
20	Photomicrograph of hyperplastic epithelium section showing immunostaining for P-CD in the basal and superficial cell layers (DAB, X40).	75
21	Photomicrograph of dysplastic epithelium section showing irregular epithelial stratification, drop-shaped retepegs, basal cell hyperplasia and hyperchromatism (H&E, X100).	76
22	Photomicrograph of dysplastic epithelium section with higher magnification showing loss of polarity, increased nuclear-cytoplasmic ratio and increased number of mitotic figures (H&E, X200).	76
23	Photomicrograph of dysplastic epithelium section showing immunostaining for P-CD in the basal and half to two thirds of the superficial cell layers (DAB, X100).	76
24	Photomicrograph showing positive reaction of P-CD in both basal and prickle cell layers masked by blue binary color to evaluate area % (X400).	77
25	Photomicrograph showing positive reaction of P-CD in both basal and prickle cell layers masked by red binary color to evaluate optical density (X400).	77
26	Clinical photograph of a 39 years old male showing a white patch on the right buccal mucosa.	80
27	Photomicrograph of hyperplastic epithelium section showing acanthosis and thick orthokeratin layer (H&E, X40).	80

28	Photomicrograph of hyperplastic epithelium section with higher magnification showing normal polarity of basal cells and normal nuclear-cytoplasmic ratio (H&E, X100).	81
29	Photomicrograph of hyperplastic epithelium section showing immunostaining for P-CD in the basal and superficial cell layers (DAB, X100).	81
30	Clinical photograph of a 53 years old male showing elevated white patch associated with smoker's melanosis on the left buccal mucosa.	82
31	Photomicrograph of dysplastic epithelium section showing irregular epithelial stratification, loss of polarity of basal cells and drop-shaped retepegs (H&E, X100).	82
32	Photomicrograph of dysplastic epithelium section with higher magnification showing increased number of mitotic figures, atypical mitotic figures, increased nuclear-cytoplasmic ratio and loss of polarity of basal cells (H&E, X200).	83
33	Photomicrograph of dysplastic epithelium section showing immunostaining for P-CD in the basal cells (DAB, X100).	83
34	Photomicrograph showing positive reaction of P-CD in both basal and prickle cell layers masked by blue binary color to evaluate area % (X400).	84
35	Photomicrograph showing positive reaction of P-CD in both basal and prickle cell layers masked by red binary color to evaluate optical density (X400).	84

List of tables

No	Heading	Page No
1	2005 WHO classification of potentially malignant lesions (<i>Warnakulasuriya et al., 2008</i>).	32
2	Criteria used for diagnosing dysplasia (<i>Warnakulasuriya et al., 2008</i>).	33
3	Descriptive data of the studied groups.	54
4	Comparison between mean optical density in normal tissues (control group) and smokers not suffering from smoker's keratosis (group II).	56
5	Comparison between mean optical density in normal tissues (control group) and smokers suffering from smoker's keratosis (group III).	57
6	Comparison between mean optical density in group II and group III.	59
7	Comparison between mean optical density of the three groups.	61
8	Comparison between mean area % in control group and group II.	63
9	Comparison between mean area % in control group and group III.	64
10	Comparison between mean area % in group II and group III.	66
11	Comparison between mean area % of the three studied groups.	68
12	Correlation between mean optical density and mean area % in each group.	70

Abbreviations

- | | |
|---|---|
| <ul style="list-style-type: none">▪ ADAM▪ AJs▪ Area %▪ CAMs▪ CDs▪ DAB▪ DD▪ DSC▪ DSG▪ E-CD▪ EGF▪ E-selectin▪ H&E▪ HHD▪ HRP▪ ICAM-1▪ ICAM-2▪ Ig▪ IgSF▪ IL-1▪ L-selectin | <ul style="list-style-type: none">▪ A disintegrin and metalloprotease domain.▪ Adherens junctions.▪ Area percentage.▪ Cell-adhesion molecules.▪ Cadherins.▪ 3-3' diaminobenzidine.▪ Darier's disease.▪ Desmocollin.▪ Desmoglein.▪ Epithelial cadherin.▪ Epidermal growth factor.▪ Endothelial - selectin.▪ Hematoxyline & Eosin.▪ Hailey-Hailey disease.▪ Horseraddish peroxidase.▪ Intercellular adhesion molecule-1.▪ Intercellular adhesion molecule-2.▪ Immunoglobulin.▪ Immunoglobulin superfamily.▪ Interleukin-1.▪ Leukocyte - selectin. |
|---|---|

<ul style="list-style-type: none"> ▪ NCAM ▪ N-CD ▪ OSCC ▪ PBS ▪ P-CD ▪ PDGF ▪ PF ▪ PS-1 ▪ P-selectin ▪ PV ▪ SCC ▪ TGF ▪ VCAM-1 ▪ VE-CD 	<ul style="list-style-type: none"> ▪ Neural cell adhesion molecule. ▪ Neural cadherin. ▪ Oral squamous cell carcinoma. ▪ Phosphate buffer saline. ▪ Placental cadherin. ▪ Platelet-derived growth factor. ▪ Pemphigus foliaceus. ▪ Presenilin-1. ▪ Platelet - selectin. ▪ Pemphigus vulgaris. ▪ Squamous cell carcinoma. ▪ Transforming growth factor. ▪ Vascular cell adhesion molecule-1. ▪ Vascular epithelium cadherin.
--	---

Contents

	page
• Introduction	1
• Review of literature	4
• Aim of the study	40
• Subjects and methods	41
• Results	51
• Discussion	85
• Conclusions & Recommendations	98
• Summary	100
• References	104
• Arabic summary	

استمارة معلومات الرسائل التي تمت مناقشتها

الكلية/المعهد: كلية طب الفم والأسنان - جامعة القاهرة القسم: طب الفم و علاج اللثة

١- الدرجة العلمية: ماجستير

٢- بيانات الرسالة:

عنوان الرسالة باللغة العربية:

ظهور جزىء الكادهرين پ- فى الغشاء المخاطى الفموى عند المدخنين.
(دراسة هستوكيميائية)

عنوان الرسالة باللغة الأجنبية

P-Cadherin Expression in Oral Mucosa of Smoker Patients.

(An Immunohistochemical Study)

التخصص الدقيق: طب الفم و علاج اللثة

تاريخ المناقشة: ٢٠٠٩/٤/١٢

٣- بيانات الطالب:

الاسم: شرين على حسن الجنسية: مصرية النوع: أنثى

العنوان: ٣٦ شارع ١٠٥ - المعادى رقم التليفون: ٢٥٢٥٢٣٧٣

جهة العمل: كلية طب الفم والأسنان - جامعة القاهرة رقم الفاكس:

البريد الإلكتروني: cherriesah@hotmail.com

٤- المشرفون على الرسالة:

أ.د. سهير محمد جعفر أستاذ متفرغ بقسم كلية طب الفم و جامعة

القاهرة طب الفم و علاج اللثة الأسنان

د. حسام الدين حسين أستاذ مساعد بقسم كلية الطب

الباثولوجيا العامة جامعة القاهرة

د. شاهيناز جمال الدين العشري مدرس بقسم طب الفم كلية طب الفم و جامعة
وعلاج اللثة الأسنان القاهرة

٥- مستخلص الرسالة (Abstract)

٥-١ باللغة العربية :

تهدف هذه الدراسة الي تقييم جزئ الكادهرين ب- عند المدخين في وجود أو عدم وجود زيادة في طبقة القرنية في الغشاء المخاطي الفموي و أيضا تقييم هذا الجزئ كعامل حساس في الغشاء المخاطي الفموي عند المدخين. وجد أن المخاط الفموي الطبيعي قد اعطي رد فعل ايجابي في الخلايا القاعدية و الخلايا ما فوق القاعدية مع النسبة المئوية للمساحة (٢٥.٩٪) و الكثافة المرئية (٢,٦٢). وجد أن النسيج الطلائي المفرط للخلايا في المجموعتين الثانية و الثالثة قد اعطي رد فعل ايجابي في الخلايا القاعدية و الخلايا ما فوق القاعدية والخلايا الحكية مع النسبة المئوية للمساحة (٨,٣٥٪) و الكثافة المرئية (٤,٧٥) في المجموعة الثانية، النسبة المئوية للمساحة (٣٠٪) و الكثافة المرئية (٣,٤٠) في المجموعة الثالثة. يرجع الارتفاع في المجموعة الثانية الي زيادة سرعة أنقسام الخلايا الطلائية. أما في المجموعة الثالثة الأنخفاض يرجع الي التحول في نوع الغشاء الطلائي الي النوع المتقرن. من الممكن الأستنتاج بأن الانخفاض المصاحب للتغيرات المتوسطة و القوية يمكن أعتباره كعامل حساس للتغيرات السرطانية.