Effect of Smoking on Skin Elastic Fibers
Morphometric and Immunohistochemical Analysis

Thesis
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Contents

List of Abbreviations

A1AT	Alpha 1-Antitrypsin
ANUG)	Acute Necrotising Ulcerative Gingivitis
BCC	Basal Cell Carcinoma
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
DAB	3, 3'-Di-Amino-Benzidinetetrahydrochloride
H&E	Hematoxylin and Eiosin
LNG	Leukokeratosis Nicotina Glossi
MAO	Monoamine Oxidase
MMPs	Matrix MetalloProteinases
mRNA	Messenger RNA
PBS	Phosphate-Buffered Saline
Pi	Protease inhibitor
PMNs	PolyMorphoNuclear leukocytes
PPP	PalmoPlanter Pustulosis
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
SI	Smoking Index
SIDS	Sudden Infant Death Syndrome
spss	Statistical Package for Social Sciences
TIMPs	Tissue Inhibitors of MetalloProteinases
US	United States
UV	Ultra Violet
WHO	World Health Organization

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Introduction

Tobacco smoking is one of the major health problems in the world and is causally related to many chronic and malignant diseases. Human skin is exposed to smoke directly through its irritant components on the epidermis and indirectly on the dermis via the bloodstream. It is not surprising therefore that smoking has many effects on the skin and is associated with significant morbidity of this organ ***(Wolf et al., 1995).***

In the past three decades, several studies have shown that smoking is an independent risk factor for the development of premature facial wrinkling and skin ageing ***(Daniell, 1971 and Leung and Harvey, 2002).***

In order to establish the pathophysiological mechanisms underlying this premature wrinkling and based on the finding that elastin is the major target in smoke-induced emphysema ***(Wright and Churg, 1995 and Vlahovic et al., 1999)*** several reports have used morphometry to analyze the elastic fibers of the skin in smokers and nonsmokers ***(Frances et al., 1991 and Lister et al., 1999).***

The results showed an increase in the number, thickness and total area occupied by dermal elastic fibers in smokers compared with nonsmokers. Another study, however, shows contradictory findings which question the effects of smoking on elastic fibres of the skin ***(Knuutinen et al., 2002).***

The hypothesis that elastin could also be the main target in smoke-induced wrinkles, as occurs in emphysema, has been supported by the fact that lung function is related to the morphological characteristics of elastic fibers in the reticular dermis, and that both characteristics depend on the amount of tobacco consumed ***(Just et al.,2005).***

Aim of the work

The goal of this study is to investigate quantitative and qualitative changes of the dermal elastic tissue of nonsunexposed skin induced by smoking, as well as the possible mechanisms responsible for them. Morphometric analyses and immunohistochemical techniques were used to assess dermal elastic fibers in a well-defined cohort of smokers and nonsmokers.

Smoking

Smoking is a leading cause of disease and death in the world ***(Kennedy et al., 2003).*** Worldwide, approximately 2 million people die every year because of smoking, half of them under 70 years of age ***(Fortes et al., 2005).***

History of tobacco Smoke:

A legend among the Huron Indians of North America tells how the Great Spirit sent a girl to restore a land ravaged by famine; potatoes grew where she touched the ground with her right hand, and, from where she sat sprang tobacco. Whatever the origins of tobacco plant, it is likely that the pleasurable consequence of inhaling its smoke were discovered more or less by chance ***(Stepany, 1980).***

The history of Western man's association with tobacco dates since 1492. King James has discouraged smoking by saying "Smoking is loathsome to the eye, hateful to the nose, harmful to the brain and dangerous to the lung ". However the habit still persists. Since the introduction of tobacco into Europe from America in the 16th century, tobacco has been used consistently in a variety of forms. The way in which it has been used has varied with decades of fashion, starting with pipe smoking, then in the 18th century snuff taking, then pipe smoking again and now predominately in the form of cigarettes. Tobacco has also been chewed, a method favored by miners when a naked light would be dangerous ***(Stepany, 1980).***

In India, “bidis" is 'the common form of smoking. Bidis -locally made cigarettes - has a high tar, nicotine and carbon monoxide content and is considered more dangerous ***(Crofton, 1990).***

In the Middle East, local smoking patterns are not confined to cigarettes; Goza and shisha are widely practiced. They are quite different from cigarettes, cigar and pipes. Goza and shisha smoking utilize the procedure of (hubble, bubble) in which the smoking sublimates are passed through a pot containing water ***(Salem, 1979).***

Prevalence:

Although tobacco may be consumed by either smoking or other smokeless methods such as chewing, the World Health Organization (WHO) only collects data on smoked tobacco. Smoking has therefore been studied more extensively than any other form of consumption ***(World Health Organization, 2009)***

In the year 2000, smoking was practiced by 1.22 billion people, predicted to rise to 1.45 billion people in 2010 and 1.5 to 1.9 billion by 2025. If prevalence had decreased by 2% a year since 2000 this figure would have been 1.3 billion in 2010 and 2025 ***(Guindon et al., 2003).***

Smoking is generally five times more prevalent among males than females; however the gender gap declines with younger age. In developed countries smoking rates for men have peaked and have begun to decline, however for women they continue to climb

(Peto et al., 2006 and World Health Organization, and the Institute for Global Tobacco Control 2009).

By the year 2002, about twenty percent of young teens found to be smoking worldwide, with 80,000 to 100,000 children taking up the habit every day—roughly half of whom live in Asia. Half of those who begin smoking in adolescent years are projected to go on to smoke for 15 to 20 years ***(Guindon et al., 2003).***

The WHO states that "Much of the disease burden and premature mortality attributable to tobacco use disproportionately affect the poor". Of the 1.22 billion smokers, 1 billion of them live in developing or transitional nations. Rates of smoking have leveled off or declined in the developed world. In the developing world, however, tobacco consumption is rising by 3.4% per year ***(Rock et al., 2007).***

The shift in prevalence of tobacco smoking to a younger demography, mainly in the developing world, can be attributed to several factors. The tobacco industry spends up to 12.5 billion dollars annually on advertising, which is increasingly geared towards adolescents in the third world because they are a very vulnerable audience for the marketing campaigns. Adolescents have more difficulty understanding the long term health risks that are associated with smoking and are also more easily influenced by “images of romance, success, sophistication, popularity, and adventure which suggests they could achieve through the consumption of cigarettes”. This shift in marketing towards adolescents and even children in the tobacco industry is debilitating to organizations’ and countries’

efforts to improve child health and mortality in the developing world. It reverses or halts the effects of the work that has been done to improve health care in these countries, and although smoking is deemed as a "voluntary" health risk, the marketing of tobacco towards very impressionable adolescents in the developing world makes it less of a voluntary action and more of an inevitable shift ***(Nichter and Cartwright, 1991).***

Genetics:

According to three separate studies commissioned by governments in the US and Europe, scientists have identified a genetic link that makes people more likely to become addicted to tobacco. This genetic variation causes individuals to smoke more cigarettes, makes it harder for them to quit and increases their likelihood of developing lung cancer by up to 80%.Genetic markers of more than 35,000 people (mostly smokers and ex-smokers) were surveyed by scientists in three separate studies, and all three found lung cancer to be associated with similar sets of genetic differences. The genetic variations of note encode nicotine receptors on cells and were identified on a region of chromosome 15***(Hung et al., 2008).***

Another study related to genetic changes in smokers was conducted by ***Lam and Lam***, in ***2007***. The study revealed that cigarette smoking can turn on or off some of the genes, which otherwise would remain inactive. Some changes on genetic level could be reversed after quitting the smoking habit, yet others could not. Examples of reversible genes involved; the so-called xenofobic functions, nucleotide metabolism and mucus secretion. Smoking

turns off some DNA repair genes that cannot be reversed. It also switches off some genes responsible for protection from cancer growth in the body.

Mortality:

According to the results of a 50 year study of 34,439 male British doctors, at least half of all lifelong smokers die earlier as a result of smoking ***(Doll et al.,2004).*** In the United States alone, cigarette smoking and exposure to tobacco smoke results in at least 443,000 premature deaths annually (***Adhikari et al., 2008)***.

Compositions of Tobacco Smoke:

Tobacco smoke comprises a volatile or gas phase and a solid or particulate phase (Table 1). The gas phase, with around 500 components, represents 95% of the weight. The particulate phase, which represents 5% of the weight, is composed of approximately 3500 constituents, the most important of which is nicotine alkaloid (figure 1) (***Just-Sarobé., 2008).***

Table (1) shows the composition of tobacco smoke *(Just-Sarobé, 2008).*

Solid Phase (Particles)	Gas phase
Nicotine	Carbon dioxide
Phenol	Carbon monoxide
Catechol	Hydrogen cyanide
Quinoline	Nitrogen oxides
Aniline	Acetone
Toluidine	Formaldehyde
Nickel	Acrolein
N-Nitrosodimethylamine	Ammonium
Benzopyrenes	Pyridine
Benzanthracene	3-Vinylpyridine
2-Naphthylamine	N-Nitrosodimethylamine
	N-Nitrosopyrrolidine

Nicotine:

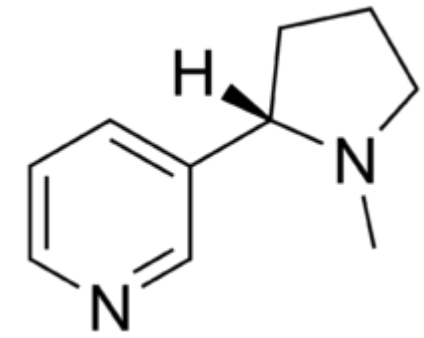

Fig 1: Nicotine molecule ***(Tsuguhide et al., 2002).***