



An Overview of iQOS® as a New Heat-Not-Burn Tobacco Product and Its Potential Effects on Human Health and the Environment

Isıtmalı Tütün Ürünü iQOS® Hakkında Değerlendirme, İnsan ve Çevre Sağlığı Üzerindeki Etkileri

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ABSTRACT

Tobacco smoke from regular cigarettes contains a number of harmful chemicals such as nicotine, arsenic, benzene, carbon monoxide, heavy metals, and tobacco-derived nitrosamines. About 1% of over 7000 chemical substances formed by burning tobacco are identified as the leading causes or possible risk factors of smoking-related diseases such as lung cancer, cardiovascular diseases, and emphysema. The concept of heating tobacco without combustion and smoke has been designed for more than two decades. The products developed with this idea, known as "Heat-Not-Burn" tobacco cigarettes, were first introduced in the late 1980s but did not achieve commercial success. However, the tobacco giants have been trying to remarket tobacco heating systems with new technological and modified features for over 10 years. I-Quit-Ordinary-Smoking (iQOS®) is one of the latest heat-not-burn tobacco products, first launched in Japan and Italy. The company then made a submission to the Food and Drug Administration as a modified-risk tobacco product application to sell its own tobacco-heating device iQOS® under its Marlboro® brand in the USA with reduced-risk claims in 2016, but it was rejected. This device is, however, now sold in more than four dozen countries. There are some striking claims that iQOS®, which is described as a novel hybrid product between traditional cigarettes and electronic cigarettes, offers an alternative way to substantially reduce the amount of harmful components compared with traditional cigarettes by its new technology in which tobacco is heated up to 350°C instead of being burnt. It is claimed to produce vapour containing nearly 90% less toxic substances than cigarette smoke and not be a source of second-hand smoking negatively affecting indoor air quality. The purpose of this article is to objectively review the potential effects of iQOS® on human health and the environment by searching and integrating the published research findings.

Key words: iQOS®, heat-not-burn tobacco products, cigarette, nicotine, smoking

ÖZ

Geleneksel sigaraların yanması sonucunda ortaya çıkan tütün dumanı nikotin, arsenik, benzen, karbonmonoksit, ağır metaller ve tütüne özgü nitrozaminler gibi birçok zararlı kimyasal içermektedir. Tütünün yanmasıyla oluşan 7000'den fazla kimyasalın yaklaşık %1'i akciğer kanseri, kardiyovasküler hastalıklar ve amfizem gibi sigara içimine bağlı hastalıkların nedeni veya potansiyel nedeni olduğu bilinmektedir. Sigara içiminde tütünün yanması yerine ısıtıldığı sistemler, yirmi yıldan fazla süredir tasarlanmaktadır. "Heat-Not-Burn" tütün ürünleri olarak bilinen bu ürünler, ilk kez 1988'de piyasaya çıkmış ancak ticari bir başarı sağlayamamıştır. Son 10 yılda, pek çok sigara firması tarafından yeni tasarımı ısıtmalı tütün ürünleri yeniden piyasaya sürülmektedir. İlk kez Japonya ve İtalya'da tanıtılan I-Quit-Ordinary-Smoking (iQOS®) için modifiye edilmiş risk tütün ürünü olarak Amerikan Gıda ve İlaç Dairesi'ne başvurusu yapılmış fakat bu başvuru reddedilmiştir. Ancak günümüzde 41 ülkede halen satışı devam etmektedir. Geleneksel sigara ve elektronik sigara arasında melez bir ürün olarak kabul edilen iQOS®, tütünün yanmadığı ve 350°C'ye kadar ısıtıldığı yeni teknolojisi ile geleneksel sigaralara kıyasla zararlı bileşenlerin seviyesinde önemli derecede azalma vadetmektedir. Tamamen iQOS®'ye geçiş yapan sigara içicilerinde birden fazla zararlı bileşene maruz kalma oranının azaldığı, iQOS® tarafından üretilen buharın sigara dumanından çok daha az toksik olduğu, iQOS® kullanımının iç hava kalitesini olumsuz yönde etkilemediği ve iQOS®'nin pasif içicilik için bir duman kaynağı olmadığı konusunda bazı görüşler mevcuttur. Bu çalışmanın amacı, iQOS® üzerine yapılan bilimsel araştırmaların incelenerek, iQOS®'nin insan sağlığı ve çevre üzerine etkilerini objektif bir şekilde ortaya koymaktır.

Anahtar kelimeler: iQOS®, ısıtmalı tütün ürünleri, nikotin, tütün, sigara

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INTRODUCTION

The combustion of tobacco generates inhalable toxic chemicals that cause some deadly diseases, notably cancer. Tobacco companies have long been developing products such as e-cigarettes and nicotine replacement therapy to prevent burning. In response to the scientifically proven harmful effects of traditional smoking, heat-not-burn tobacco products as a new attack by the tobacco industry are gaining popularity and taking over the markets. While hot debates still continue over the use of such devices, Philip Morris International (PMI) has embarked upon marketing a new generation heat-not-burn tobacco product, called I-Quit-Ordinary-Smoking (iQOS®), which is claimed to have revolutionary technology that heats tobacco instead of burning it. PMI claims that this product gives the real taste of tobacco with no fire, no ash, and less smoke as well as eliminating the undesirable effects related to smoking by reducing the levels of toxic chemicals.¹ iQOS® consists of three main components: a tobacco stick (called a HeatStick), a battery-powered tobacco heating holder, and a charger. It is used by inserting the disposable tobacco stick into a slot and then heating it at temperatures below 350°C. The holder provides heat to the tobacco unit for about 6 min or 12-14 puffs. The most important difference between iQOS® and traditional cigarettes is that while tobacco in a regular cigarette is burned at above 600°C, iQOS® just heats tobacco up to 350°C. It has long been said that iQOS® does not release smoke containing unhealthy components due to not burning tobacco at high temperatures, and it prevents users from being exposed to the same levels of carcinogens and toxic chemicals found in a conventional cigarette.^{2,3}

More than \$3 billion has been spent over a 10-year period in research and development to design and produce new devices like iQOS® according to PMI's statements, and pilot schemes for iQOS® began in Italy and Japan during late 2014.² However, Food and Drug Administration (FDA) approval was required to market the device in America as a less harmful product than continuing to smoke cigarettes in accordance with its commercial purposes. PMI filed modified risk tobacco products (MRTP) applications MRTP for three different iQOS® cartridges (Marlboro HeatSticks, Marlboro Smooth Menthol HeatSticks, and Marlboro Fresh Menthol HeatSticks) with the US FDA on 5th December 2016. PMI's claims in this application are as follows: completely switching from cigarettes to iQOS® considerably reduces the risk of tobacco-related diseases and would cause less harm than regular smoking by significantly preventing exposure to harmful or potentially harmful chemicals.^{4,5} The FDA's Tobacco Products Scientific Advisory Committee discussed the MRTP applications in January 2018 and rejected the proposal that iQOS® should be marketed as healthier than traditional cigarettes in the US,^{6,7} but the product is currently being sold in more than 40 countries.²

There is no legal regulation in respect of using iQOS® in this country. Smoking accounts for 27% of deaths⁸ and 120.000 people (one person every 5 min) die every year in Turkey due to tobacco and tobacco-related diseases. Therefore, all kinds of legislation of practice that this country will put into place

regarding cigarettes and tobacco products are of utmost importance. Turkey has been fighting a running battle against tobacco since 2008. As smoking-related regulatory efforts have been correctly addressed to achieve sustainable progress, Turkey has become the first country to achieve the highest level of implementation for all six World Health Organization (WHO) tobacco control policy measures (Monitor, Protect, Offer, Warn, Enforce, Raise). After the implementation of comprehensive laws in 2009, the overall rate of smoking, which was 31.2% in 2008, decreased to 27% in 2012⁹ and 23.8% in 2015, and it is estimated that this rate will drop to 19% in 2025 in Turkey.¹⁰ In addition to these advances, the exposure prevalence in workplaces and restaurants decreased considerably from 37% and 56% in 2008 to 16% and 13% in 2012, respectively. Despite the smoking ban in enclosed public spaces in Turkey, the rate of passive smoking is still over 50% in total because exposure to smoke in homes is quite high (38.3%).¹¹ Cigarette smoke, also called passive smoke or environmental tobacco smoke, contains 72 fully characterized carcinogens¹² as well as at least six toxic substances that are toxic to reproduction. Second-hand smokers inhale the combination of the smoke exhaled by an active smoker and the smoke from the burning cigarette, and they are more exposed to these toxic chemicals than regular smokers. Furthermore, there is no known safe level of exposure to passive smoking.¹³ Legal regulation is therefore necessary for iQOS®, which does not have a risk assessment in this country.

As iQOS® has a short (4-year) history, there are not enough studies on its effects on human and environmental health. As investigations on iQOS® were carried out only by the producing company and its competitors in those years and this has driven the need for more independent scientific data about its safety, the number of studies on this product has been increasing considerably in recent years. Given the discouraging laws that are enforced in many countries to protect people from passive smoke of tobacco products, the claims that iQOS® does not release harmful fumes makes it an attractive device to smokers, and the adverse health effects will be reduced if the tobacco is consumed only by heating without burning. The hazardous constituents of tobacco smoke are related to the intake of a large number of chemical substances resulting from the completed combustion (pyrolysis) and heat decomposition (thermogenic degradation) of tobacco. Eight volatile organic compounds and 13 polycyclic aromatic hydrocarbons (PAHs) are released by iQOS®. Although almost all of them are present in moderately to greatly lower amounts than in conventional cigarettes, a number of cancer-causing chemicals are still present in iQOS® emissions. The levels of nicotine, benzaldehyde, and formaldehyde were 84%, 50%, and 74% of those from a typical cigarette, respectively. However, acenaphthene was found at levels 295% of that released from a regular cigarette and its effects on human health are not known. Based on the fact that the idea that there should be a threshold value for the toxic effects of passive smoking should be rejected, according to Principle 1 for implementing article 8 of the WHO convention on tobacco control, it is argued that iQOS® cannot be considered

as a different product from traditional cigarettes and this device should fall under the same smoking bans for regular cigarettes.¹⁴

Based on the claim that iQOS® can prevent passive smoking, Protano et al.¹⁵, in 2016, compared the profiles of passive smoking exposure by measuring the submicron particles (SMPs) generated by the use of traditional cigarettes, iQOS®, and electronic cigarettes. SMPs emitted from traditional and hand-rolled cigarettes during smoking and also accumulated in the respiratory system of passive smokers were observed four times higher than those released from electronic cigarettes and iQOS®. These particles produced by conventional and hand-rolled cigarettes have been found to remain for a long time in the environment after smoking. It has been reported that the concentrations of these particles, which are emitted from electronic devices and iQOS®, rapidly return to their previous state and their mean diameter increases by combining with each other, and therefore they precipitate immediately. In addition, SMPs produced as a result of combustion have been observed to maintain their dimensions and therefore they have been suspended in the air for a long time. It was also stated that about half of these accumulated particles were small enough to reach the alveoli of passive smokers.¹⁵ Contrary to this research showing that iQOS® smoke can be less harmful than traditional cigarettes, Bekki et al.¹ found different findings for iQOS® in 2017. In that study, the harmful compounds such as nicotine, carbon monoxide, tar, and tobacco-specific nitrosamines in iQOS® tobacco and smoke were explored and their concentrations were compared with those in reference cigarettes such as 1R5F and 3R4F. The nicotine concentration in iQOS® tobacco and smoke was almost the same as that of traditional cigarettes, and nitrosamine and carbon monoxide were found at levels of one-fifth and 1% that of regular cigarettes, respectively. Toxic compounds have been reported to be present in iQOS® vapour, even though at low levels.¹ Farsalinos et al.¹⁶ demonstrated that the nicotine concentrations in iQOS® tobacco sticks are roughly similar to those of traditional cigarettes and are higher than those of electronic cigarettes when the puff time is short.¹⁶ On the other hand, the size and volatility characterization of the particles were also calculated by measuring their concentration and distribution in iQOS® aerosol. The particle concentration in iQOS® smoke was less than 1×10^8 particles/cm³, but their size distribution was found about 100 nm. However, it has been shown that as the temperature rises, the particle size distribution drops roughly to 20 nm (300°C) and the volatility of particles increases. The amount of nonvolatile particles breathed by iQOS® users was calculated as 1-2 mm² per puff in regard to the surface area of the particles. This was 4-fold higher than the amount inhaled by electronic cigarette users.¹⁷

It is predicted that there may be a positive correlation between the use of this product and the occurrence of respiratory diseases. A study evaluating the relationship between iQOS® and the expression of nasal platelet activating factor receptor (PAFR), which affects the adhesion of bacteria causing respiratory tract infection, observed that PAFR expression significantly increased in nasal epithelial cells after iQOS® exposure and bacterial adhesion to nasal epithelial cells thus

increased.¹⁸ In particular, that study also provided evidence that the use of iQOS® increased the vulnerability to respiratory tract infections and infection-induced asthma attacks. Sohal et al.¹⁹ investigated the effect of e-cigarettes, tobacco smoke, and iQOS® on human lungs *in vitro*. The data obtained from their study show that mitochondrial respiration function alters in consequence of iQOS® exposure, as in e-cigarette and traditional cigarette exposure. Mitochondrial dysfunction may further lead to respiratory infections, airway remodelling, and lung cancer by stimulating epithelial mesenchymal transition, as seen in chronic lung diseases. iQOS® is also thought to enhance infections by increasing microbial adhesion to the airway. Their study highlighted for the first time that exposure to iQOS® smoke is as harmful as that to cigarette and electronic cigarette smoke for human lung cells.¹⁹

There are also very limited scientific data about the potential effects of iQOS® on the environment. Given the fact that air pollution caused by cigarette smoke is ten times higher than that created by a diesel engine,²⁰ it is of great importance to identify the possible harmful effects of iQOS® on the environment. In this regard, when the emission factors of many air pollutants were calculated to quantify harmful compounds released to the atmosphere, the metal emission values for iQOS® were relatively low compared to traditional and electronic cigarettes. However, some *n*-alkanes and organic acids have been emitted in significant amounts, whereas PAH compounds could not be detected in iQOS® smoke. Even though the emission of these toxic compounds is lower than that of traditional cigarettes, this product is not without risk to the environment.³

According to the results of a survey on awareness and use of this new tobacco product offered for sale under striking advertising slogans such as Heat-Not-Burn, approximately 20% of the 3086 participants aged 15 and over had knowledge about iQOS®. While the number of nonsmokers among the people who had previously tested iQOS® was similar to that of active smokers, the number of nonsmokers who wanted to try this product was higher than that of the current users.²¹

Since iQOS® is a new device, it is assumed that there will be some risks related to its use. When the possible risks of the filter and its cleaning on human health are examined, the polymer film filter in the tobacco unit is observed to easily melt during use (90°C), and even though in low amounts formaldehyde cyanohydrin, which is a very toxic substance, is formed. Researchers have highlighted that iQOS® is not just a product that only heats tobacco because iQOS® tobacco appears charred, and this toxic compound also increased when it was not cleaned after each use. The product has also been reported to have limitations that would affect the application of ISO 3308 standard smoking protocols.²²

CONCLUSIONS

In order to make a general conclusion about iQOS®, which is described as a device that combines technology with tobacco, there are not enough research-based findings yet. Especially taking into account that it is a youth-appealing product with its

technological design, there are big concerns owing to the fact that there is no universally accepted risk assessment behind it. In contrast to the company's claims, the presence of PAHs in IQOS® aerosol can be a sign of burning tobacco. Although it is still unclear what the exact harmful effects of this device are, there is a small consensus that it is less risky than continuing to smoke cigarettes. However, it is also underlined that toxic chemicals are still present in IQOS® smoke and the product could lead to people taking up smoking cigarettes. Therefore, more scientific research data are needed to reach an objective conclusion about the effects of IQOS® on human health and the environment. The best way to protect people from passive smoke is to encourage active users to quit smoking completely.

Conflict of Interest: No conflict of interest was declared by the authors.

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