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The ban of eletronic cigarettes in Brazil: success or failure?

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Abstract *Brazil was one of the first countries in the world to ban Electronic Smoking Devices (ESDs). This ban was motivated by the lack of evidence regarding the alleged therapeutic properties and harmlessness of these products. Anvisa was criticized for this move, especially by electronic cigarette's users groups. These groups argue that prohibition prevented people's access to a product that would aid smoking cessation and be less toxic than ordinary cigarettes. Thus, the question arises as to whether this decision was successful. Available data show that ESDs have diverse formulations and some toxic substances are released at significant levels during use. Studies in animals and humans have shown a potential toxic effect, also affecting the health of passive smokers. Studies are still inconclusive regarding its use as a cessation tool. A high level of use among adolescents was observed in countries whose use was authorized. Thus, Brazil's ban prevented the population from consuming a product that has not been proven effective toward smoking cessation, with indications of significant toxicity and highly attractive to young people.*

Key words *Smoking habit, Tobacco-derived products control and oversight, Tobacco products, Vapers, Vaping*

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Introduction

The National Health Surveillance Agency (Anvisa) was established by Law 9782/1999[1], and regulation, control and oversight of control products and services that pose a risk to public health (Art. 2, subsection III and Article 7 subsection XV) are among its various attributions (Art. 8). Cigarettes, cigarillos, cigars and any other fumigant products, whether or not tobacco-derived (Art. 8, § 1, subsection X) are within the scope of products subject to health surveillance.

The emergence of so-called electronic cigarettes and reports of use of these products in Brazil[2] led Anvisa to issue in 2009 Resolution RDC 46/2009[3] prohibiting the sale and advertising of any Electronic Smoking Device (ESD) with or without nicotine throughout national territory until scientific studies and toxicological and clinical evaluations are performed, aiming at identifying its risks and alleged effectiveness in smoking cessation. In addition to the lack of scientific studies, Anvisa also considered in the ban the harmful potential of nicotine's purified extracts to human health.

Thus, Brazil was one of the first countries in the world to ban Electronic Smoking Devices (ESDs)[3], popularly known as electronic cigarettes (which are actually just one of several types of known ESDs, but which in this text can be considered as synonyms).

The National Health Surveillance Agency (Anvisa) was highly criticized for this ban, especially from user groups. These groups accused (and still accuse) Anvisa of having banned a product that would aid smoking cessation and would be less toxic than ordinary cigarettes, so that this prohibition would not be reasonable from the health viewpoint, besides having no basis scientific evidence[2,4].

Recently, according to a personal communication from the Anvisa's General Manager of Tobacco Products, the tobacco industry joined enthusiasts to pressure Anvisa to release these products. Allegations are the same as those used over 8 years ago, that it would be a safer product and help smoking cessation.

Thus, this text aims to discuss the main aspects raised by ESD advocates and to evaluate whether regulation implemented by Anvisa is effective from the viewpoint of public health.

Methods

This paper was written by using PubMed (Medline)[5] and SciELO[6] databases to search for scientific articles and Google Search Engine[7] to search for reports, legislations, stories and others documents.

We selected only full-text papers available on the Internet and published in English, Spanish or Portuguese. References were collected from March to September 2017. Papers duplicates and studies totally or partially funded by the tobacco or ESDs industry were also excluded.

In databases of scientific papers, free terms (without use of controlled vocabulary - Descriptors) were used, as a result of the different indexing processes, besides providing a greater retrieval of papers, reports and other types of publication within the criteria used. The terms Tobacco use disorder, Tobacco Smoke Pollution, Tobacco Use Cessation, Electronic Cigarettes, Tobacco Use Cessation Products, associated with the qualifiers Adverse effects, trends, health effects, composition, utilization, children, teenager, second hand smoke, epidemiology, accidents and Brazil were used.

Function, composition and toxicity of ESDs

ESDs are battery-powered electronic vaporizers[8]. Despite their various generations, the basic structure consists of a nozzle (inhalation nozzle), cartridge location or solution tank (depending on model), atomizing element, microprocessor, battery compartment and, in some cases, a LED light on the tip[9] (Figure 1).

When using the product, the user presses a button or activates a pressure sensor by inhalation, the atomizer heats and atomizes the tank or cartridge solution. The solution is heated to temperatures between 100-250º C to generate the aerosol[10], popularly called vapor[11]. ESDs products are today in their 4th generation[12], where new technologies have been incorporated, as shown in Chart 1, even Bluetooth technology to answer phones through the equipment is available[13]. Products of all generations are currently found on the market[12].

The literature shows that e-liquids used in the ESDs are quite different in terms of chemical composition, nicotine concentration and additives used[14]. The literature also shows a discrepancy between the composition stated on the package and the actual composition of the prod-

uct[11]. About 8,000 electronic cigarette flavors have been described[15].

Propylene glycol and glycerol are the major components of ESDs liquids (e-liquid). Exposure to propylene glycol can cause eye and respiratory system irritation and, in the event of chronic exposures, affect the nervous system and spleen. When heated and vaporized, it can generate propylene oxide, which is classified as 2B carcinogen by IARC[16,17]. To date, no studies demonstrating the formation of this substance in ESDs have been identified. In the case of glycerol, the heating process would be related to the formation of acrolein, a known upper airway irritant, where some studies point to the formation of this agent in the vapor of ESDs[16,18].

Studies have also described that electronic cigarettes would release some toxic substances, such as formaldehyde, acrolein, acetaldehyde, propanol, nicotine, tobacco-specific nitrosamines and particulate matter, usually with much lower concentrations of these agents than those found in traditional cigarettes[12,16,19-32]. However, Jesen et al.[33] demonstrated that the new generation of electronic cigarettes in some situations (high-voltage devices) would expose e-cigs smoker to doses of formaldehyde 5 to 15 times higher than the concentrations found in common cigarettes. We must certainly consider that these studies were conducted in the laboratory and in conditions that could be difficult to reproduce in real life. In addition, the puff regime and the analytical methods used in the available studies vary widely, which makes their comparability difficult. Therefore, caution should be exercised in the analysis and comparison of these results.

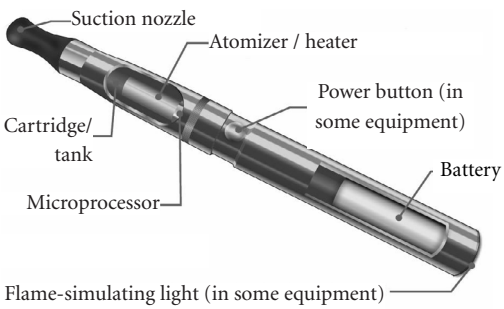

Figure 1. Parts of an Electronic Smoking Device.

Chart 1. Characteristics of ESDs.

Generation	Type of equipment	Structure	Battery (mAh)	Observations
1st	Single-use ESD	Single piece	90-200	Cartridge
			Fixed voltage	
	Rechargeable battery	Reusable battery/ Single -use cartridge	90-200	Cartridge
			Fixed voltage	
	Three-piece tank system	Separate battery, atomizer and tank	90-200	Tank
			Fixed voltage	
2nd	Reusable/replenishable ESD	Separate battery and tank	300 - 1100	Tank/ Variable voltage
			Variable voltage	
	Reusable/replenishable ESD	Separate battery and tank	300 - 1100	Tank/ MODs (user fills the tank with solution that he can prepare)
			Voltage and power based on battery output	
3rd	Reusable/replenishable ESD	Separate battery and tank	300 - 1100	Tank
			Variable voltage and power	
4th	Reusable/replenishable ESD	Separate battery and tank	>1000	Tank/Temperature control/ some models are equipped with Bluetooth technology
			Variable voltage, power and temperature	

Source: Modified from (12).

Table 1 shows the composition of cartridges and aerosol of selected substances compared to conventional cigarettes.

In vitro and animal studies show some toxic effects and that toxicity varies depending on the flavor additives used in e-liquids. Compared with

Table 1. Comparison of selected chemicals found in ESDs and conventional cigarettes.

	Matrix	Electronic cigarettes	Conventional cigarettes
Nicotine	Liquid	0 – 50 mg/ ml (composição do e-liquid)	0,8 – 2,3 mg/g
CO	Aerosol	<0.1 mg/99 puffs	10–23 mg/cigarette
Aldehydes			
Formaldehyde	Aerosol	Low voltage 3.3V – ND	3 mg/day (20-unit pack)
		High voltage 5V – 14.4 +- 3.3 mg day (3 ml of fluid) / Type of vapor – More efficient deposition in the respiratory tract	
Acetoaldehyde	Aerosol	0.11–1.36 µg/ 15 puffs <LQ – 11 mg/m3	18-1400 µg/cigarette
	Refill solution	0.10 – 15.63 mg/L	
Acrolein	Aerosol	<LQ – 4.19 µg/ 15 puffs	2.4-62 µg/cigarette (fume)
o-methyl benzoaldehyde	Aerosol	1.3 - 7.1 µg/15 puffs	ND
Acetone	Aerosol	2.9 mg/m^3	50 – 550 µg/ cigarette
Tobacco-specific nitrosamines			
NNN	Aerosol	0.00008–0.00043 µg/15 puffs	0.005–0.19 µg/ cigarette
	Aerosol	<LD – 4.3	
	Refill solution	0.34 – 60.08 µg/L	
NNK	Aerosol	0.00011–0.00283 µg/15 puffs	0.012–0.11 µg/cigarette
	Refill solution	0.22 – 9.84 µg/L	
NAT	Refill solution	<LD – 62.19 µg/L	0.3 – 5 µg/cigarette
NAB	Refill solution	<LD – 11.11 µg/L	109 – 1,033 µg/cigarette (NAB + NAT)
Metals and metalloids			
Cadmium	Refill solution	0.42 – 205 µg/L	0.5 – 1.5 µg/cigarette
Nickel	Refill solution	58.7 – 22,600 µg/L	0.078 – 5 µg/cigarette
Lead	Refill solution	4.89 – 1,970 µg/L	1.2 µg/cigarette
Chrome	Refill solution	53.9 – 2,110 µg/L	0.0002–0.5 µg/cigarette
Manganese	Refill solution	28.7 – 6,910.2 µg/L	155 – 400 µg/g
Polycyclic aromatic hydrocarbons and cresol			
Cresol	Aerosol	0.16 ppm/ 38 ml puff	11-37 µg/cigarette
Anthracene	Aerosol	7 µg/ cartridge	24 µg/cigarette
Phenanthrene	Aerosol	48 µg/ cartridge	77 µg/ cigarette
Pyrene	Aerosol	36 µg/ cartridge	45–140 µg/ cigarette
Volatile organic compounds			
Toluene	Aerosol	0.02 – 0.63 µg/15 puffs	8.3 – 70 µg/cigarette(fume)
p, m Xylene	Aerosol	<LD – 0.2 µg/15 puffs	366 µg/cigarette
Propylene Glycol	Aerosol	1,660 – 5,525 µg/puff 59 – 67% 21 – 82% of the refill's composition	1 – 2 mg/ cigarette
Glycerin	Aerosol	5 – 15 µg/puff 21 – 82% of the refill's composition	1 – 2 mg/ cigarette

NNN - N-nitrosonornicotine; NNK - 4-(methylnitrosamin) 1 - (3- pyridyl)-1 –butanone; NAT - N-nitrosoanatabine; NAB - N-nitrosoanabasine, <LQ – Below the quantification limit; <LD – Below the detection limit; ND – Not detected.

Sources: (11,12,16,19,23-33).

conventional cigarettes, the effects of these emissions would be less toxic[34-37].

Effects of ESDs on humans

In humans, reports from users indicated irritation in the mouth and throat, coughing, headache, dyspnea and vertigo[38]. Another study suggests a potential carcinogenic effect of electronic cigarette emissions[39]. There was also a significant increase in nicotine and cotinine levels in the saliva and urine of electronic cigarettes users[20,40-42], in some cases comparable to traditional cigarette smokers[40]. Passive smokers of electronic cigarettes also had increased levels of cotinine and nicotine in urine[43,44]. A study also suggests that e-liquids flavors can affect the rate of nicotine absorption in humans and contribute to the acceleration of increased heart rate and other subjective effects described among users[45].

One study observed acute pulmonary effects, pulmonary impedance, resistance to peripheral airflow and oxidative stress after 5 minutes of electronic cigarette use[46]. Another study pointed to the reduction of forced expiratory volume[47].

Regarding the health effects in humans in the long term, there are no studies to that effect, due to the fact that they have been on the market for a relatively short time.

Other health hazards

Another relevant point of electronic cigarettes is the increasing number of cases of intoxication by accidental ingestion of their cartridges, especially among children[48]. Searching for *Brazilian Toxicological Information System*[49] and news on the Internet, there were no reports of accidental intoxication by e-liquids in Brazil.

Another risk to its users and those close to them is the risk of explosion of the batteries of these devices, and there have been reports of injuries and fires caused by the explosion of ESD batteries, usually occurring while these devices were being charged[9,50].

Environmental Tobacco Pollution

Regarding environmental tobacco pollution, studies have shown that concentrations of toxic substances to which passive smokers are exposed is up to 10 times lower than that of conventional cigarettes. However, we should remember that these same studies pointed out that passive smokers are still exposed to toxic substances such as nicotine 1,2 propanediol and particulate matter[43,47,51,52]. Therefore, the use of these products in collective use environments is not recommended, since even at lower levels, toxic substances found in the emissions of these products have potential harm to health[16,21,43,52-55] and are still a potential source of third-hand contamination[56]. The concept of third-hand smoke or contamination applies when the smoker releases nicotine while exhaling smoke (or vapor), and this is impregnated on surfaces and objects, persisting for months in these environments. Because of this, reactions occurred between environmental pollutants and compounds emitted by the smoker. One of the components formed from these reactions would be the tobacco-specific nitrosamines[57].

ESDs as smoking cessation aids

Looking at the literature on electronic cigarettes as an alternative to smoking cessation, studies seem to suggest a slight increase in cessation rates among users of electronic cigarettes. However, published data are not sufficient to state that electronic cigarettes would be an effective method to stop smoking[50]. Questions are also raised about the impact of these products on the cognitive behavioral approach, as they are not inducive to the self-assessment and self-monitoring experience, reinforcing the idea that it is still premature to consider these products cessation-effective[50]. No study was found to evaluate the cost-effectiveness of these products in smoking cessation.

In relation to cessation, the case of England, which, based on a report commissioned by Public Health England, (agency linked to the Ministry of Health of that country), may recommend the use of electronic cigarettes as smoking cessation aid[58].

This report concludes that ESDs would be 95% less toxic than conventional cigarettes; they would be helping to reduce smoking rates among young people and could be effective in smoking cessation[58]. One of the authors went further and stated that the ESDs could be: *a watershed in public health, in particular because of the reduction of the enormous health inequalities caused by smoking*[59].

However, this report was heavily criticized by an editorial in Lancet[60] for basing its main conclusion (that ESDs would be 95% less toxic than cigarettes) by ignoring the caveats made by authors of the main study[61] (two studies were used, one of which is a short 4-page report to the

English Parliament[62]) which substantiated this conclusion that there was no solid evidence for assessed harm and that there was no formal criterion for the recruitment of experts, or in the words of the Lancet editor: *the opinions of a small group of individuals with no prespecified expertise in tobacco control were based on an almost total absence of evidence of harm*[60].

In addition, the editorial notes that this same study was funded by the manufacturers of ESDs[60], which raises substantial issues about conflicts of interest involving the main bibliographical reference of the English report.

Use and marketing of ESDs

Observing data on the use of electronic cigarettes in countries where the marketing of these products is released, a high degree of experimentation and use among youngsters[16,63,64] is observed, and in some countries such as Poland and the United States, more than 1/3 of the young people have already experienced ESDs[64,65]. Studies also show a significant frequency of double users[64,66]. A meta-analysis published in 2017 also points out that adolescents who use ESDs are four times more likely to be at risk of smoking traditional cigarettes than those who do not use these devices[67].

In the United States, the use of electronic cigarettes, among high school students, increased from 1.5% in 2011 to 20.8% in 2018[68]. Among elementary school students, the use of these products increased from 0.6% in 2011 to 4.9% in 2018[68]. In short, almost 1 in 5 American high school students makes use of electronic cigarettes[68]. For this reason the US government has declared that the use of electronic cigarettes among young people is an epidemy[69]. The rapid growth in consumption of these products could be caused by the introduction of new products with new nicotine manipulation technologies[70].

In addition, smoking experts have stated that there is no treatment for nicotine addiction caused by this new generation of electronic cigarettes in adolescents to date[71].

Data about the use of electronic cigarettes in in Brazil is very limited and indicates that 4.6% of adult smokers have tried cigarettes or used electronic cigarettes in the last 6 months (the study did not distinguish between experimentation and continuous use)[72]. Another study carried out in university students revealed that 2.7% had tried it, and 0.6% had regular use of it[73]. No studies were found on the use of ESDs among children or adolescents in Brazil. The use of other types of ESDs in Brazil has also not been reported. The ban could explain the reduced use of these products in Brazil.

Studies on the use of ESDs in Brazil[72-74] have shown that the prevalence of use of these products was the lowest among countries participating in the International Tobacco Control Survey (ITC), but their use in life was not so different when compared to these other countries. Another important finding of the study is that a significant fraction of smokers, independent of country or level of regulatory restriction, believed that ESDs were safer than conventional cigarettes[72,74].

World ESD regulations

Research conducted by the World Health Organization[75] has shown that the regulatory approach between countries is very diverse, and more than half of the countries have no regulation or at least no specific regulation exists. In Brazil, these products are classified as tobacco-derived products[3].

Probably because of this regulatory diversity and the different legal and regulatory frameworks of countries, the World Health Organization does not indicate how these products should be classified but, on the other hand, understands that these products should be within the scope of the Framework Convention on Tobacco Control and which have the potential to weaken tobacco control policies if they are not effectively regulated[75-77].

Although there are natural differences in the way that ESDs are regulated, the fact that these products are regulated especially in regard to the harmful potential of nicotine and its capacity to cause dependence and so as to prevent these products from interfering negatively in tobacco control policies (free environments, as a gateway for new smokers, interfere with cessation, etc.) is undisputable[16,75-78].

Final considerations and conclusions

More than eight years after its banning and revisiting the scientific literature in search of some new data that could lead to a possible revision of the standard, the same questions that led to the prohibition of these products still continue without a response capable of fulfilling the regulatory requirements for the release of these products in Brazil.

While data suggest lower toxicity of these products than traditional cigarettes, they could not be considered harmless either. However, a question arises where we weigh a possible harm reduction: "What is the acceptable harm reduction standard of a product that simulates smoking? Considering that cigarette toxicity is so high, it is relatively easy for something to be less toxic than conventional cigarettes, but this doesn't mean that it does not pose a threat to human health".

The enormous variety of flavors, the different compositions and toxic emissions of the ESDs indicate that the regulation of these products in a possible release of sales should be carried out case by case and not broadly, without considering the different formulations, types and voltages applied.

By prohibiting these products, Brazil prevented the population from consuming a product whose alleged smoking cessation assistance has not been confirmed, with indications of significant toxicity. It also prevented young people from experimenting with this product.

We can thus consider that, for the Brazilian tobacco control setting, the benefits of this ban outweighed by far and were more significant than the supposed and unproven benefits of the release of these products. Thus, we can consider that Anvisa's decision was correct and the motivation of banning these products remains valid, thus contributing to the already recognized success in its tobacco control policies.

Collaborations

ALO Silva and JC Moreira worked on conception, research, methodology and final writing.

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