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Editorial

E-Cigarette: "Harm Reduction Tool" or "Facinating Killer Device"

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E-Cigarettes is an innovative electronic device simulating conventional cigarette, which neither burn or produce smoke nor contain solid particles or tar. According to few researchers it is considered to be safe, consequently, became the commonly used smoking products worldwide, especially among youth, with more than a 9-fold increase in usage from 2011 to 2015. However its safety profile is still under scan by the global research fraternity and statement that vapor generated by E- cigarette, absolutely safe, is not true [1,2]. The basic concept of E-cigarettes was coined by Herbert Gilbert in 1963. In 2003, a Chinese pharmacist Han Li obtained a patent for "a non-flammable electronic atomizing cigarette" and in 2004, the Ruyan Company of China started to develop as well as sell E-cigarettes commercially. While in 2007, the international patent of E-cigarettes was gained, and product gradually circulated into Europe and America [3].

E-cigarette atomizes the liquid in the cartridge, produced vapor will enter the body through the mouth [4]. With regard to their design, and there are four generations of devices currently in the market. The first-generation e- cigarettes are the "cigar-like" devices; they are constructed of a cartomizer (cartridge and an atomizer) with a low-voltage battery (3.7V). Second-generation e-cigarettes are bigger in size with a refillable tank; their battery voltage is adjustable, allowing users to use low or high voltage (3 - 6V) during vaping. The third-generation devices are also known as mods and have the largest size batteries, with voltages up to 8V. The fourth and most recent generation includes Sub ohm tanks (devices whose atomizer coils have a resistance of less than 1 ohm) and temperature control devices, which allow for temperature modulation during vaping [2]. E-liquids, are now available in more than 7,000 unique flavors, including cherry, bubblegum, and chocolate. E-liquids contain nicotine along with flavorings, propylene glycol, glycerin, and other ingredients like aluminum (Al), arsenic (As), cadmium (Cd), copper (Cu), iron (Fe), manganese (Mn), nickel (Ni), lead (Pb), and zinc (Zn), formaldehyde, and hydrocarbons [5,6].

In humans, e-cigarettes induce acute symptoms of nausea, headache, cough, and throat irritation, similar to nicotine patches, while adolescents using e-cigs reported an overall increased rate of chronic bronchitis symptoms. Though tar and other harmful ingredients have been removed, its safety is questionable, due to the existence of nicotine and other potential hazards such as aerosol particles and different flavor additives in the e-liquid. It was cited that some E-cigarettes produce more particles than traditional cigarettes which may lead to increase risk of cardio-respiratory morbidity as well as mortality [2,7]. According to recent literature flavorings may also induce lung inflammation. Diacetyl present in many e-cig liquids (found in caramel, butterscotch, watermelon, pina colada, and strawberry) cause of bronchiolitis obliterans (popcorn lung) [8,9]. Recent research reveal that e-cig liquids with flavors like cherry yield increased amount of benzaldehyde, in addition Cinnamon-flavorings had the most cytotoxicity among 36 different e-liquids; the constituents in the cinnamon-flavored liquids thought to be responsible for the cytotoxicity were cinnamaldehyde (CAD) and 2-methoxycinnamaldehyde (2MOCA). According to eminent researchers several flavorings induce expression of inflammatory cytokines in lung cell cultures, where acetoin and maltol are among the most potent [10].

Currently, much of the evidence regarding effects of e-cigs comes from cell culture and animal studies. Normal human bronchial epithelial (NHBE) cells exposed to e-cig aerosols, with or without nicotine, increase IL-6 and IL-8 cytokine levels. Another study reported a

change in the gene expression pattern of NHBE cells with silenced p53 and activated KRAS when exposed to e-cig aerosol. Apart from this, e-cig liquid was assessed in NHBE cells in parallel with a knock-out mouse model; there were increased rates of infection, inflammatory markers and altered gene expression [11]. Metals present in e-cig aerosol are capable of causing cell injury and inflammatory cytokine induction, e.g. in human lung fibroblasts. There have been some studies of gene expression in cultured human bronchial epithelial cells showing changes in profiles that are much less than smoking but clearly distinctive [3].

The study of Gases showed that the mixture of the formaldehyde, acetaldehyde and acrolein generated during heating of glycerol found in E cigarette, produced more sensory stimuli than those of a single compound. Among them, formaldehyde was categorized as a Class 1 carcinogen in 2006. Acrolein stimulates the nasal cavity, damages the lungs and the inner walls of the blood vessels, as well as recognized as a major factor leading to cardiovascular disease. Chronic inhalation of acrolein inhibits circulation of endothelial progenitor cells and promotes atherosclerosis, which accelerates the rate of hardening of the aorta by 1.6 times. In the study of Czogala J., *et al.* and Goniewicz ML., *et al.* endorse that toluene and meta xylene were detected in almost all sample smokes. These VOCs are irritating to the skin and mucous membrane, as well as have anesthetic effects on the central nervous system, along with certain carcinogenicity [2]. The chemical mixture in the smoke of the E-cigarette will cause chromosome division, and may cause damage to mitotic spindles or filaments, thereby inducing mutations. In 2013, Williams M., *et al.* found heavy metals such as tin, nickel, lead, chromium and other nano particles in the smoke of E-cigarettes can be deposited in the alveoli, inducing lung damage and leading to cough, dyspnea, chest pain, pulmonary edema, acute respiratory failure, as well as carcinogenicity, nephrotoxicity, and neurotoxicity [10,12,13].

It is now an open secret that, secondhand smoke produced by traditional cigarettes has many effects on human health, including increased risk of respiratory tract diseases, lung cancer, infectious diseases, acute cardiovascular diseases, and cerebral apoplexy, which is mainly the side-stream smoke [10]. However, the E-cigarette does not produce side-stream smoke, In the study of Flouris AD., *et al.* and colleagues, 15 non-smokers were exposed to secondhand smoke from traditional cigarette or smoke from E-cigarettes for an hour, and then the cotinine levels in their serum were tested. The results showed that the cotinine levels in the serum of non-smokers were similar after inhaling the secondhand smoke of traditional cigarettes and E-cigarettes (2.6 to 2.4 ng/mL). As a result, nicotine levels, along with levels of some potentially toxic substances in the body, will increase when they are exposed to the second hand smoke of E-cigarettes. Although current studies have shown that the risk of secondhand smoke generated by E-cigarettes is expected to be lower than that of traditional cigarettes [3].

It was cited that E-cigarettes are effective for some people to achieve smoking cessation. However, the review included 24 completed studies: 21 cohort studies; 2 RCTs comparing e-cigarettes with placebo e-cigarettes (i.e. without nicotine), with a combined sample of 662 participants, in which the 6-month quit rates were 9% with e-cigarettes and 5% with the placebo device; and a third RCT, which compared e-cigarettes with a nicotine patch and found no difference in quit rates at 6 months [14]. In addition to this, some people may become a "double user", namely they smoke both traditional cigarettes and E-cigarettes, especially in places where smoking traditional cigarettes is prohibited. This does not help to quit smoking, rather leads to greater harm from smoking. E-cigarettes may also be a potential way for adolescents or non-smokers to use tobacco. Moreover, users of E-cigarettes are less likely to quit smoking than those who have never used it [15,16].

Therefore harm of E-cigarettes cannot be underestimated. *In vivo* and *in vitro* evidence has revealed that the components contained are harmful to the Cardio-respiratory system. Under the current circumstances, it is of great importance to investigate the impact of E-cigarettes or e-liquid on human health rigorously to avoid its irrational use by the young population in different part of the world due to lack of evidence based knowledge, whether it is genuinely "Harm reduction tool or merely a killer device".

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