REVIEW / ARTÍCULO DE REVISIÓN

Probe on Various Experimental Cigarette Smoke Subjection Structure

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DOI. 10.21931/RB/2022.07.02.8

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Abstract: Different methods of subjection to smoke from experimental cigarettes are essential for understanding tobacco smoke. The major toxicants found in tobacco are acetaldehyde, acetone, acrolein, acrylonitrile, ammonia, benzene, cadmium, catechol, chromium, cyanide hydrogen, arsenic, nickel, nitric oxide, nicotine last but not least, mono-oxide gases. While experts say, cigarette smoke contains more than 4000 different compounds. These are substantially toxic and can destroy cells, and many of them are carcinogenic. Various smoke-exposure devices are used for in-vitro tobacco smoke generation, dilution, and distribution.

Such devices are used widely by well-known manufacturers or can be tailor-made setups. We can set up different in-vitro models to better treat smoke-related diseases using these subjection structures. The fundamental goal will be to build a tobacco-free society of available subjection systems. Some have been identified and established as biological endpoints in some published scientific literature. In the scientific field, many new technologies are coming out and showing their presence. There are many systems of exposure to cigarette smoke in vitro which offer a more flexible approach to the challenges of exposure to tobacco smoke. This review covers some topics such as the description of available new subjection structures and reviews their work, setting up and application for Scenarios of in-vitro treatment. The benefits and disadvantages of both subjection mechanisms and the similarities between the setups and the data extracted from these structures. Measuring the smoke dose is also discussed here as an important field of research, particularly in the preclinical phase.

Key words: Cigarette smoke, Cigarette Subjection Structures, Cigarette Subjection Mechanisms, Cigarette Subjection Advantages, Cigarette Subjection Use, Cigarette Subjection Modern advancements.

Introduction

Most findings of respiratory disease relate specifically to tobacco consumption. Comprehension of the complex dynamics of tobacco smoke is fundamental, which can allow the precursors and mechanisms responsible for adverse health effects[1]. The smoke from tobacco kills up to half its users. More than 8 million people are killed by cigarettes each year. About 7 million of those deaths result from direct use of cigarettes, while about 1.2 million results from second-hand smoke exposure by non-smokers[1,4,6]. Tobacco causes severe injuries to the health because of hazardous chemical compounds such as nicotine, cadmium, lead, polonium-210, benzene, acrylonitrile, various aldehydes, aromatic amines, aromatic polycyclic hydrocarbons[2,6]. The compositions are related to COPD, lung toxicity, and multiple cancers.

In-vitro tobacco smoke measurement is conducted on the particulate process collected on a Cambridge filter pad and eluted in DMSO or bubbled through the media or PBS to cell culture[3]. The cell cultures are then exposed to the particulate phase under submerged conditions. Sadly, particulate-based exposures do not consider the period of cigarette smoke vapor or the related interactions between the level of particulate matter and vapor[3,4]. Aquatic agricultural environments and particulate-based concentrations do not match the human lung's primary stream exposure to tobacco smoke. Separating fractions of smoke in this manner could also contribute to alterations[5]. The chemical changes may not indicate the smoke aerosol as a whole. Whole smoke exposure systems were developed to overcome the problems[6]. Different whole-smoke exposure systems are available worldwide, and most of them in Germany is very popular. There must be some drawbacks, but they could play an important role and bridge the gap between technologies, not only in calculating the actual cell dosage but also in characterizing and validating these systems[5,7]. A review article covers recent advances in various subjection systems for cigarettes, their mechanisms of action and their application in different fields[3,7]. These are very useful for understanding the processes of the cell damage and disease mechanisms caused by tobacco[8]. This review describing tobacco smoke and disease, elucidating disease processes and defining smoke toxicants responsible for adverse health effects will be critical in-vitro approaches using dose instruments will add strength to the in-vitro data resulting from this[9].

Whole Smoke Exposure Systems

Traditional techniques of exposure to smoke are based on the particulate phase of cigarette smoke and omit any subsequent analysis of the vapor and semi-volatile phase. Whole smoke exposure systems allow evaluating all stages of smoke together or separately, depending on the experi-

Citation: Das, Moulima.; Saha, Anupam., Probe on Various Experimental Cigarette Smoke Subjection Structure. Revis Bionatura 2022;7(2). 7. http://dx.doi.org/10.21931/RB/2022.07.02.7
Received: 10 June 2021 / **Accepted:** 24 January 2022 / **Published:** 15 May 2022

mental setups[5,7,10]. This has enabled researchers to conduct their experiments to investigate tobacco smoke phases, yielding valuable information. Some of the systems on the market include Bespoke[11], Borgwaldt[12], Burghart[13], Vitrocell[14], and Cultex[15]. Among these is the more advanced Vitrocell system. A summary of different whole smoke exposure systems can be found in table 1.

Vitrocell Systems

A brief detailing with advancements of Vitrocell systems where now a days this is the advanced in-vitro exposure systems. The system's goal is to assist in attaining the research goal by working hand in hand with the researchers. This integral commitment to one's research means one can count on the system to propose optimally tailored components[40], provide the latest installations[41], an international training and a world-class service precisely to the requirements of the researchers.

Vitrocell Inhalational Toxicology

They advanced device systems for in vitro characterization of airborne substances at the air / liquid interface, such as gases, complex mixtures, nanoparticles and fibers. The device design considers the type of aerosol, the insert sizes of the cell culture, the mammalian cell system and the dosimetry. The details of this type are illustrated in table 2, table 3 and table 4, respectively[45-47].

Classification of Vitrocell systems [42,43,44]

Vitrocell system

- Inhalational toxicology
- Skin exposure
  - a) Vitrocell skin module
  - b) Skin max module
  - c) Cloud skin
  - d) Skin autosampler
- Auxiliary equipment

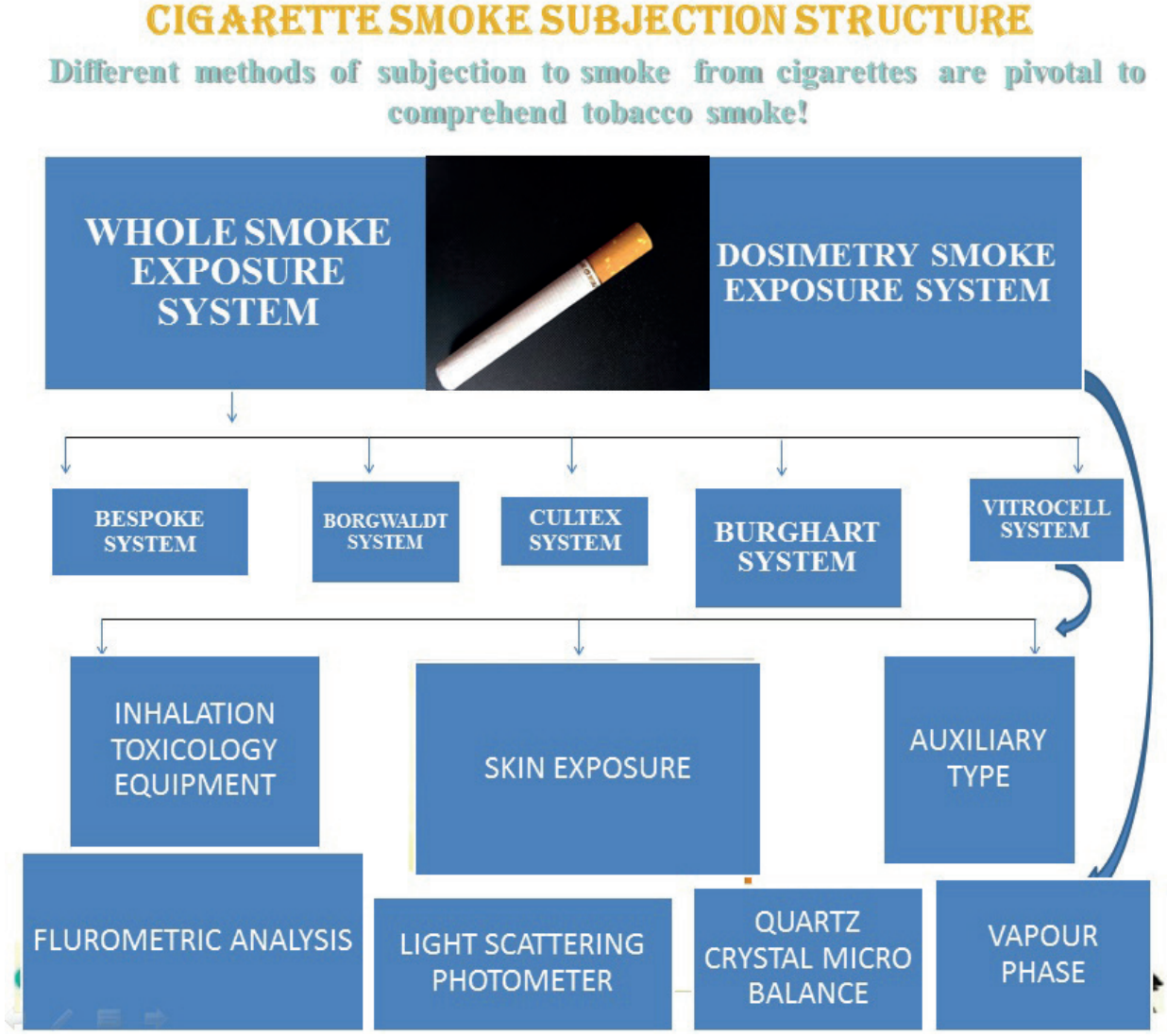


Figure 1. Graphical abstract on various cigarette smoke subjection structures.

	2.1 Bespoke System	2.2 Borgwaldt System	2.3 Burghart System	2.4 Cultex System
Another Name	-	Borgwaldt RM 20S [16] (Borgwaldt KC Gmbtt, Hamburg, Germany.	The Burghart Mimic Smoker MSB-01 (Burghart Tabaktechnik, Wedel, Germany) [16,17]	Cultex Laboratories (Hannover, Germany) [18]
Parts of the System	a) Hermetic chamber b) Two large ventilation holes c) Cell culture plate d) A small fan [19].	a)8 syringes b)Cigarette smoke generator c)A syringe based dilution system d)Additional 4 syringe unit e)Airflow controller f)Cell culture media g)Chamber house h)Smoke diluter [19,20]	a)Integrated multi format b)96 micro well format c)Simplistic chamber d) An independent exposure module [28].	a)Hyp-hydraulic press b)Cultex dust generator c) Integrated elutriator [31,32].
Mechanism	Exposure of cells to smoke for two days followed by assessment of cell supernatant by enzyme linked immunosorbent assay. Then comparison of results [21].	Smoke generation by syringe followed by a puff of filtered air for dilution. Exposure of diluted smoke into the chamber followed by dilution of smoke and cellular exposure between 12 and 24s depending on solution [22,23].	Doses of cigarettes will be assessed by independent syringes, followed by the dilution capability up to 1:150. A consistent exposure is provided across the multiwall plate. At last, the disclosures of cigarette puffs are taken for approx. 6s [29,30].	a)Particle deposition assessment by fluorescence spectrophotometer b) This module is useful in response to mainstream cigarette smoke and deducing a possible mechanism for losing tight junction stability in the respiratory epithelium in smokers [33,34].
Uses	-	a)Product assessments b)Fundamental research [24]	-	a)In-vitro toxicological substances of air-bone substances b)Research related inhalational toxicology c) Access a multitude of smoke-related research [35,36].
Advantages	a)Non-expensive b)Easy maintenance c)Simple structure d)Sophisticated design e) Unique nature of smoke generation, dilution and exposure characteristics [24].	a) Rotary style structure b)Capable of smoking up to 8 cigarettes simultaneously c) No cross cigarette contamination [26].	a)High throughput in-vitro experimentation [30].	a)Precisely control system b)Provide homogeneous distribution c)Trumpet technology facilitates aerosol delivery directly onto the cell monolayer d) Very useful for Ames test [37].
Advancement	Set up maintaining 3D arrangement of the human mucosa and allow a quasi-replication model of the inhalation/exhalation cycle [24,25].	The interchangeable system, an essential system of in-vitro development and machine characterization papers [27].	-	a)Easily understand a disease mechanism b)Useful tool to assess therapeutic efficacies in-vitro c) Latest development is the radical flow system [38,39].

Table 1. Comparison between different types of whole smoke subjection structures.

Method	Exposure system	Aerosol and gas supply	Aerosol generator	Smoking machine	Dilution	Humidification	Dose monitoring
Air/liquid interface	a)Modules for 6 well inserts b)Modules for 12 well inserts c)Modules for 24 well inserts d)Modules for 35mm Petri-dishes e)Modules for suspension cells f)Modules for 96 well inserts g)Vitrocell cloud system h)Vitrocell powder chamber i)Automated exposure system	a)Aerosol generator b)Smoking machine	1)Bioaerosol nebulizing generator 2)VAGF nebulizing generator 3)VAGK nebulizing generator 4)VRGB generator	1)VC1 type 2)VC1S type 3)VC1/7 4)VC10 5)VC10 S type 6)Chem control feature 7)Human puff profiles 8)Vitrocell vapestrater	a)Gas distribution system b)Only dilution system c)HD distribution system d)Sidestream chamber	a)Humidification station b)Washing bottle c)Inline humidifiers	a)Microbalance sensor and software b)Photometer and software c)Filter housing d)Co-monitoring e)Vitrocell FT-IR f)Vitrocell photon ion

Table 2. Details of vitrocell inhalational toxicology system.

Bio-aerosol nebulizing generator	VAGF nebulizing generator	VAGK nebulizing generator	VRGF generator
Nebulizes clean liquids, solutions and suspensions.	Available and reproducible particle size (<2 micron) by cyclone.	Nebulizes clean liquids and different concentrated solutions.	Dispersion of non-cohesive powders and dusts of particle sizes <0.1 micron to 100 micron.
Ideal for proteins, bacteria and micro-organisms.	Nebulizes clean liquids, suspensions and solutions.	Long dosing time	Optional cyclone for particle sizes <5 micron.
Approx. particle diameter is 0.7 to 2.5µm. Low flow rate with optional precision pump.	Long dosing time. Distribution system designed for vitrocell modules.	HD distribution system designed for Vitrocell modules. -	Very constant output and good reproducibility. Variable mass flow and HD distribution system designed for Vitrocell modules.

Table 3. Some features of the aerosol generator systems used in Vitrocell systems[48,49].

Vitrocell Skin Exposure Systems

High tech equipment solutions for the exposure of skin tissue to solid, liquid or gaseous substances. VITROCELL Skin modules are a powerful alternative to glass-made Franz cells as they offer improved handling, higher throughput and options for automation[53-55].

Vitrocell Auxiliary Equipment

A range of durable components for a successful and long-lasting operation of our exposure systems. Own equipment solutions were developed when commercial solutions are not available. VITROCELL approved auxiliary equipment fits perfectly into our turnkey installations[56].

Name of the Section	Types	Uses
Aerosol and gas supply	Aerosol generator Smoking machine	For liquids, suspensions, solutions and dry powders Well suited for e-cigarettes
Smoking machine	VC 1 type VC 1 S type VC 1/7 type VC 10 type VC 10 S type Chem control feature Human puff profiles Vitrocell Vapestarter	For conventional and electronic cigarettes with high technical features For manual smoking For linier smoking For fully automated smoking robot For high end smoking robot For fully automated smoke lung robot Option for Vitrocell smoking machine Innovative solution for the button activation of e-cigarettes
Dilution	Gas distribution system Only dilution systems HD distribution systems Side stream chamber	For clean air and gases For dilution of gases, mixtures and conventional exhaust For testing and dilution of atmospheric substances
Humidification	Washing bottle Inline humidifiers	For simple solution of initial tests For humidification of the test atmosphere directly before exposure
Dose Monitoring	Microbalance sensor and software Photometer and software Filter housings Co-monitoring Vitrocell FT-IR Vitrocell photon ion	For high precision mass determination in ng resolution For inline assessment of particle concentration without aerosol loss For gravimetric methods For monitoring of Co in the gas phase. For online gas analysis of e-cigarettes For fast online measuring system of chemical gas analysis

Table 4. Different parts and their uses of Vitrocell Inhalational Toxicology[50-52].

Sr No.	Type	Parts of the Machine	Features
1	Vitrocell skin module	a)Base module with the cover unit and exposure top b)Controller for magnetic stirrer c)Skin module illustration d)Tissue holder with an extraction tool e)Holder compartments	i)Durable and long-lasting design ii)Unique tissue holder iii)Permanent or static medium supply iv)Integrated water bath heating circuit v)Suitable for diverse tissue thicknesses up to 2000µm vi)Exposure top for the analysis of volatile compounds
2	Vitrocell skin max module	a)Skin max module compartment b)Skin max module cover fixation bracket	i)Durable and long lasting system with integrated water bath heating circuit ii)Suitable for the tissue diameter of 50mm iii)Tissue exposure surface diameter is 25mm
3	Vitrocell cloud skin	a)Tissue holder with extraction tool b)Full set of holder counter parts	i)Exposure system for liquid aerosol ii)High droplet output rate with cloud dynamics iii)No external air flow required iv)No humidity control required v)Easy handling of unique tissue holder vi)Small residual volume in nebulizer reservoir
4	Vitrocell skin auto sampler	a)8 chamber capacitors b)Water bath heating circuit c)Magnetic stirrer d)8-stopper motor controlled individual syringes e)Magazines	i)Ideal tool for toxicokinetic study ii)High reproducibility results iii)Programmable sample volume of 0.1 to 1.0ml iv)Bubble free automated delivery of fresh receptor fluid with high reproducibility v)Possibility to integrate impedance measurements

Table 5. The various types, their parts and some essential features.

Dosimetry for smoke exposure systems

This system is essential for understanding exactly which components of smoke are exposed to the culture of cells. Tobacco smoke has two phases that can cause injury to the lung and damage to cells[60]. The dosimetry system is thus helpful in understanding the characteristics and interactions of both steps[61]. The different tools are used for particle deposition assessment under dosimetry are-fluorometric analysis[62], light scattering photometers[63], quartz crystal microbalance[64], and vapor phase[65].

Recent findings on different issues of the whole smoke exposure system

These subjection structures may be too unique in their evolution to be widely used for a consistent approach. No commercially available or otherwise available exposure system has yet been fully characterized or validated, and each system offers unique advantages and inconveniences[17]. Interestingly, an assessment by the Cooperation Authority for Scientific Research Relative to Tobacco (CORESTA) on various whole smoke exposure technologies – a tobacco-related task force in vitro, found remarkably consistent results, indicating the similar performance of these systems (CORESTA air-liquid interface report). Entire smoke exposure systems are an important development for producing an in vitro physiologically relevant test smoke aerosol[18]. In support of this, the Committee on Mutagenicity in the UK reviewed the field of 'chemicals in food, consumer goods, and the environment' in June 2009 and commented that the implementation of whole-smoke exposure protocols was likely to provide more specific data on tobacco smoke's mutagenic effect, but noted that none of the test systems

Sr. No.	Equipment parts	Components
I)	Flow measurement and control [57]	Vacuum flow calibration, Mass flow meter, Mass flow controller
II)	Clean air purification station [58]	Pressure regulator, Pre-filters with condensate trapping, Membrane dryer, Activated control filter, Fine filter
III)	Temperature control [59]	Water bath, High-performance water bath
IV)	Vacuum pump	-
V)	Precision pump system	-
VI)	Vitrocell epithelix nanopress	-
VII)	Aero list	-

Table 6. The details of the equipment are given below.

Sr No.	Name	Mechanism	Uses	Advantages
3.1	**Fluorometric analysis (Wet chemistry technique)**[64,66]	Pre-wet cell cultures are kept within the exposure chamber followed by the whole main stream smoke. Then deposited particulate materials are exerted by HPLC and analyzed with fluorescence detection along with graph generation (Fig-2a)	Quantification of particulate deposition	a)Simplistic approach b)Used in a variety of studies c)It can be applied to any subjection structure format d)Results are relatively consistent
3.2	**Light scattering photometers** [67]	Inline measurement of the particle droplet suspended in the gas via a light scattering optical sensor (Fig-2b)	Useful for in-vitro and in-vivo studies	a)Measurement of optical density at low flow rates b)No loss of particle mass c)Acts as a real time monitoring tool d)Results are always consistent and reproducible
3.3	**Quartz crystal microbalance** [68,69]	Works via piezoelectric effect and measures and detects changes in mass in the nanogram range	Investigates deposition data from a variety of cigarettes	a)It can control exposure based on particulate dose b)Modern technique consists of a gravimetric unit of deposited mass per surface area for more accuracy
3.4	**Vapour phase** [70]	Vapour phase quantification by infrared gas analyzers. The markers can be quantified inline or remotely.	Analysis of vapor phase components using chemistry trapping setups that measures phase dilution	It can quantify carbonyls in tobacco smoke easily but has many limitations.

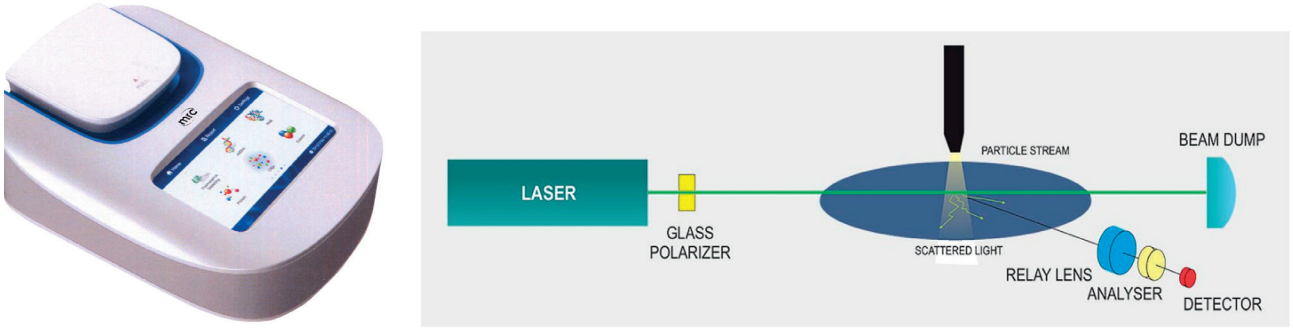
Table 7. Several dosage tools available for particulates and vapors are explored in more detail.

had been 'successfully validated'[32]. Validation remains a prominent area for improvement in this research field, and no one has yet carried out a multi-laboratory or multi-system study. Several models, techniques, findings, limitations, and further suggestions are explored in more detail in Table 8. Quartz crystal microbalance takes advantage of the piezoelectric character of quartz to characterize the formation and structural properties of thin films in real-time. This is done by simultaneously measuring the changes in the resonant frequency related to the mass/thickness of the film in contact with the surface and energy dissipation associated with the rheological properties of the adsorbed film, induced by adsorption/desorption processes or by structural changes produced within the thin film[68]. The 4-sensor chambers of the Q-Sense E4 enable the performance of four simultaneous measurements under controlled experimental conditions (temperature, flow rate), increasing reproducibility and decreasing experiment duration[69]. Also, different coatings (gold, silicon dioxide, titanium, hydroxyapatite) can be used, broadening the application field of the technique.

The scientific literature covering whole smoke structures in vitro has provided a variety of related biological endpoints, illness, and toxicology. For instance, in vitro tobacco smoke has been shown to induce various cellular effects potentially associated with disease processes, including the up-regulation of a series of factors related to lung damage and inflammation[40]. It has also been shown that tobacco smoke produces high levels of reactive oxygen species and oxidative stress that may cause cellular damage to lipids, proteins and DNA Moreover; it has been shown that cigarette smoking has several effects on gene expression in the human airways. Studies of bronchial epithelial cells obtained by bronchial brushing from smokers 'and non-smokers' airways have shown that cigarette smoke induces metabolizing and redox genes, tumor suppressor genes, and oncogenes alongside inflammatory process control[68].

Discussion

Different smoke exposure systems have already been published in various investigative journals. With respiratory conditions such as asthma and COPD symptoms increasing worldwide, many new up-gradations associated with these subjection structures are launching in the commercial markets. Such severe respiratory diseases caused by in-



a) b)

Figure 2. (a) Fluorometric analysis (Wet chemistry technique): A susceptible instrument, the wet-chemistry-based fluorimeter, is a reproducible instrument used for all fluorometric applications. The key advantages are precision and versatility[64]—four fluorescent channels in common nucleic acids and protein assays. Fluorimeters based on wet chemistry can ultimately personalize the measuring applications[66]. This instrument has powerful software and full network integration to handle the data seamlessly. This figure is obtained from MRC Laboratory-Instruments, (Available: https://www.mrclab.com/portable-fluorometer-uv-blue-channels); (b) Light scattering photometers: Light scattering photometer is essential to determine absolute molar masses from cigarette ignition. (Molar mass range-200 to million g/mole and 10nm to 50nm roots means square radii). It is an excellent method for characterizing polymer and protein in different inquiries, or product quality controls[67]. This figure is obtained from Holmarc Opto-Mechatronics PVT Ltd, Available: https://www.holmarc.com/scattering_photometer_-_single_channel_light_detection.php).

halable pollutants, such as tobacco smoke, diesel exhaust, or other sources of pollution[70,71]. Therefore, a substantial effect on national health systems is expected, indicating the long-term treatment, with routine tests accompanied by high costs[4,71]. In this context, in vitro approaches can help develop more efficient protocols, such as evaluating new compounds' toxicity during the research and development process[56]. This research will aim to better select substances suited to further development and a final reduction in the number of animal experiments[67]. Hence, researchers have developed an in vitro exposure device that allows the examination of inhalable compounds for their pharmacological and toxicological effects. There are various options for using the different smoke exposure systems to produce a steady supply of cigarette smoke with slight variations over an extended period[71]. A unique feature of the smoking systems is the conditioning and mixing chamber, which sets the primary concentration and provides a steady amount of "feed smoke" for the exposure components. Measuring and monitoring the flow rates to the exposure chambers is essential for controlling smoke levels. Any process or a mixture of measurements in the exposure portion is highly desirable for the continuous smoke concentration measurement[71]. Carbon monoxide measurement can be an anchor measurement and can be reported as a record of exposure concentration over time. During treatment, measurement of different concentrations of smoke components should be carried out on a regular schedule[70,71]. In an experiment involving the generation of smoke over prolonged periods, well-defined and documented exposure must be created. Smoke exposures are manpower-intensive and require continuous monitoring throughout the exposure cycle to maintain a steady supply of smoke[71].

Cleaning them regularly also is essential to prevent tar buildup. The smoking machine crashes and gets out of balance when pieces of tobacco and paper hit the sliding parts, and tar builds up[71]. The efficiency will improve considerably as the user becomes more familiar with aligning and keeping the system clean. If carried out correctly, an experiment with a known exposure level will be conducted with good documentation of the smoke level, which is monitored very well from day[67]. A great deal of advanced subjection structure for tobacco smoke is now used for a few days. Scientific knowledge has been published in various journals on these systems, and biological endpoints have been described. They are new to the research field and continue developing their presence[8,59].

Conclusions

Subjection structures for in vitro smoke occupy a role in fundamental and mechanical science. Various scientific literature showed the wealth of associated biological endpoints, disease, and toxicological data. Using such structures, multiple advances in vitro test methods are a promising sign and suggest that these devices can support and supplement several potential exposure scenarios. Depending on the equipment used, the ratio of smoke to air, the flow rate of mixing air added to the smoke diluter, and the fraction of smoke, in-vitro exposure systems can be viewed in many ways. Dosimetry is the most common and influential of all the methods for evaluating in-vitro tobacco smoke. The dosimetry method can bridge the gap and play an essential role in calculating and validating the actual cellular dosage. Different in-vitro models were developed based on exposure systems useful for evaluating tobacco smoke's biological activity. To understand tobacco smoke and disease and the mechanisms of disease and classify smoke toxicants responsible for severe medical conditions, in-vitro approaches will be necessary, ensuring the related exposure system is appropriately characterized.

Author Contributions

Moulima Das: Literature Review & Investigation, Software, Data Curator, Visualization, Graphs and Table preparation, Writing – Original Draft Preparation & corresponding author. Anupam Saha: Writing – Reviewing and Editing, Acquiring Permissions, Reformatting, Correction, Software and other essentials.

Serial No	System Name	Author/Year	Model Name	Technique Used	Key Findings	Limitations Suggested by the Author	Further Works Suggested by the Author
1) a.	Bespoke system	St.Laurent et al.,(2009).	Isolated rat bronchial epithelial cell model	"Harmetic" chamber used to accommodate cell culture plate following by the assessment of ELISA technique	I.MCP-1 release was inhibited II.IL-10 production was reduced.	VEGF showed no difference in production	Different models can influence the data and modulated bronchial epithelial cell mediator production differently Precautions required for choosing the models
1) b.		Gualerzi et al.,(2012)	3D *In-Vitro* set up	3D arrangement of human mucosa and quasi replication process of the inhalation/exhalation cycle	The keratin protein(K14) Was over expressed as early as after smoke exposure	Only *In-Vitro* work is done here so *In-Vivo* work is needed	
2) a.	Borgwaldt system	Phillips et al., (2005).	Bronchial epithelial NCI-H292 cell model	Cells exposed to cigarette smoke using RM 20S and BAT exposure chamber	Study demonstrates cytotoxicity, particulate deposition m-RNA and protein expression in response to tobacco smoke		-
2) b.		Maunders et al., (2007).	Bronchial epithelium cell model	Affymetrix and microarray technology	Gene expression changes	The down-regulated responses in cell adhesion may provide a possible mechanism for the permeability induced by smoke and may entail the development of various diseases caused by tobacco smoke.	British American Tobacco has used the method primarily making clear comparisons with other studies difficult.
3	Burghart system	Adamson et al., (2011b). Scian et al., (2009).	High throughput *In-Vitro* experimentation	96-micro well format of high throughput screening	Checking of cellular viabilities and smoke loss measurement	At the air-liquid interface, the cells are not supported and some implication is set up, such as smoke collection chamber, mixing bag etc.	This is simplistic cellular study so higher research related studies are required
4	Vitrocell system	Okuwa et al., (2010).	Chinese hamster lung model	Induction of micro-nuclei in hamster lung following exposure to mainstream cigarette smoke using multiple smoking regimens.	Okuwa and colleagues noted differences in micronuclei in smoking induction schemes as well as differences in the particulate and vapor phases of mainstream cigarette smoke and found robust and repeatable data	Vitrocell 10 has several variables that can be altered to establish the correct exposure setup and this is changing a recent study has evaluated these variables in the exposure module on particle deposition. An increased module flow rate in the exposure module had an inverse effect on particulate deposition	-
5	Cultex system	Aufderhlide et al., (2011).	Human bronchial epithelial 16HBE cell model	"Trumpet" technology where the human cells are exposed to cigarette smoke	Cytotoxic responses were noticed here	-	-

Table 8. Models with techniques, findings, limitations, and further suggestions.

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Funding

Authors declare that there is no such funding related to this article.

Acknowledgments

It is the wealth of experience and knowledge that is generated within the portals of NSHM Knowledge Campus, Group of Institutions-Kolkata, West Bengal, which enlightened my path to complete this manuscript. Authors would like to owe a special sense of gratitude and deep regards to the following people at Elsevier: David Throne and Jason Adamson. Without their support, we could never be able to complete this topic. The view and information of these authors have made substantial contributions to conceptions and designs have been involved in drafting the manuscript.

Conflicts of Interest

Authors declare that there is no conflict of interest.

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