Physicochemical Characterization of Air Particulate Matter in Medellin City and Its Use in an In-silico Study of the Effect of a PM Component on Cardiac Electrical Activity

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Abstract. Particulate matter (PM) is considered the most severe environmental pollution problem due to its serious effects on human health associated with an increased risk of cardiovascular morbidity and mortality. One of the most polluted cities in America is Medellin. Physicochemical characterization of PM is necessary to understand its toxicology in particular cities. The goal of this work is to perform a physicochemical characterization of PM in the city of Medellin. Lead (Pb) was chosen between the major PM components to perform an in silico study of the effect of Pb on cardiac electrical activity. Results evidence the nature of the main components present in the PM and their wide range of sizes and morphologies. Pb showed a pro-arrhythmic effect on cardiac electrical activity through shortening of APD_{90}, during normal electrophysiological conditions. In silico studies may help to better understand the mechanism of how air pollution could trigger cardiac diseases.

1. Introduction

Environmental pollution is responsible for around 4.3 million premature deaths each year [1]. In particular, air pollution increases the risk of mortality from cardiovascular disease by 76% [2]. Particulate matter (PM) is considered the most severe environmental pollution problem due to its serious effects on human health [3,4]. PM air pollution is associated with an increased risk of cardiovascular morbidity and mortality [5–10].

High levels of air pollution have been recorded in many countries around the world. In South America, specifically in Colombia, Medellin appears as one of the most contaminated cities [11,12] and some studies measuring the air quality in Medellin showed that PM concentrations are exceeding the limits defined by the WHO [13,14].

It is well known that the nature of the PM (physical-chemical characteristics) is directly related to its emission source, each region worldwide has specific characteristics associated with the type of sources present in the emission of these particles. In this way, physicochemical characterization of

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PM is necessary to understand its toxicity in a particular city [15], so a local characterization of PM has a great importance for the understanding the effects related to the region particularities. In Colombia there have been few studies of PM characterization, a study conducted in the city of Bogotá, determined that the highest metals content in the PM was mainly related to lead (Pb) and iron (Fe) [16].

Despite there are studies on the pollutants effects on the cardiovascular system, the pathophysiological mechanisms of the PM effects on cardiac electrical activity remain largely unknown. Nowadays, in silico studies (via computational simulation) have served to approximate, among other aspects, the biophysics of cardiac activity in normal and pathological physiological conditions [17–20].

In this context, the aim of this work is to perform a physicochemical characterization of PM in the city of Medellin. Results were used in an in silico study of the effect of one of the most problematic metal found in the PM components on cardiac electrical activity; contributing to the knowledge about the physiopathological mechanisms by which atmospheric pollutants can affect human health, specifically cardiovascular health.

2. Methods

2.1. Particulate Matter physicochemical characterization

PM was collected by extracting it the filters from sample of particles an environmental monitoring station in the city of Medellin. Two samples of PM were collected in different climatic conditions at a monitoring point in a residential area during a period of one month.

A physicochemical characterization of the obtained PM was carried out, through the scanning electron microscopy technique SEM-EDS. Field emission scanning electron microscopy (FE-SEM) and energy dispersive X-Rays spectroscopy (EDS) analyses were carried out in a JEOL JSM-7100F electron microscope, equipped with a silicon drift detector for EDS (X-MaxN, Oxford). Previous to the analyses, in order to improve the electrical conductivity of samples, they were coated with gold in a sputter coating system (Q300TD, Quorum).

2.2. Human cardiac cell model

Courtemanche [17] membrane formalism was implemented to simulate the electrical activity of human cardiac cell. The transmembrane voltage (V_m) is given by:

$$C_m \frac{dV_m}{dt} + I_{ion} + I_{st} = 0 \quad (1)$$

Where C_m is the membrane capacitance (100 pF), I_{ion} is the total membrane current, and I_{st} is the external stimulus current. The model is considered under normal electrophysiological conditions.

2.3. Model of PM component effect on cardiac electrical activity

Based on the results of the characterization shown in the "results" section, where lead (Pb) appears as one of the main components, and according to the results of a study in ventricular myocytes, which indicate that Pb affects the cardiac electrical activity by blocking the L-type calcium channels (I_{CaL}) [21], we developed a basic model of the Pb effect on I_{CaL} using the steady state fraction of block (b_{Pb}). Hill equation has been used to fit the concentration-response relationships for ligand block. It describes the fraction of the macromolecule saturated by ligand as a function of the ligand concentration; it is used in determining the degree of cooperativeness of the ligand binding to the receptor. In this model the kinetics of the channel would be considered unchanged in the presence of the Pb.

$$b_{Pb} = \frac{1}{\left(1+\frac{IC_{50}}{(D_{Pb})^{h}}\right)} \tag{2}$$

Where IC_{50} is the half maximal inhibitory concentration for the current block by Pb, D_{Pb} is the Pb concentration. A Hill coefficient (h) of 1 indicates completely independent binding. For the IC_{50} to block I_{CaL} we used 152 nM, this value was found by [21] in ventricular myocytes.

Following, the equations to calculate I_{CaL} are given by:

$$I_{CaL} = (1 - b_{Pb})g_{CaL}dff_{Ca}(V_m - 65) \tag{3}$$

Where g_{CaL} is the maximum conductance of I_{CaL}, d is the activation gate, f is the voltage-dependent inactivation gate, f_{Ca} is the calcium-dependent inactivation gate and 65 is the value of equilibrium potential for calcium.

2.4. Simulation protocol

Unicellular model was implemented to simulate the sinus rhythm under physiological conditions, using the Cellular Open Resource public CellML OpenCOR® software. Forward Euler method with a time step of 0.001 ms was implemented to solve the equations. A train of 10 stimuli was applied at a basic cycle length of 1000 ms. Pb concentrations from 0 to 300 nM were implemented. The APD at 90% of the repolarization (APD_{90}), I_{CaL} and the resting membrane potential were measured on the 10th beat using a program developed in MATLAB® software.

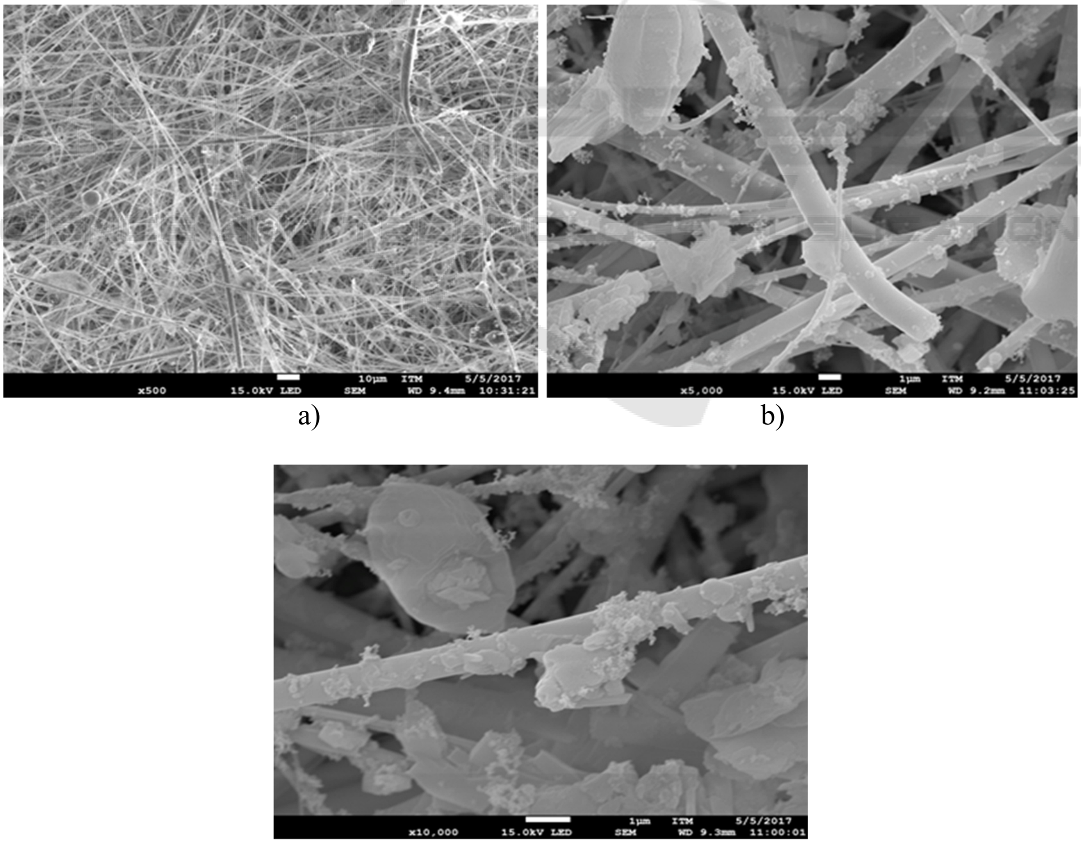


Figure 1. SEM images of filters with PM. a) X500, b) X5000 and c) X10.000.

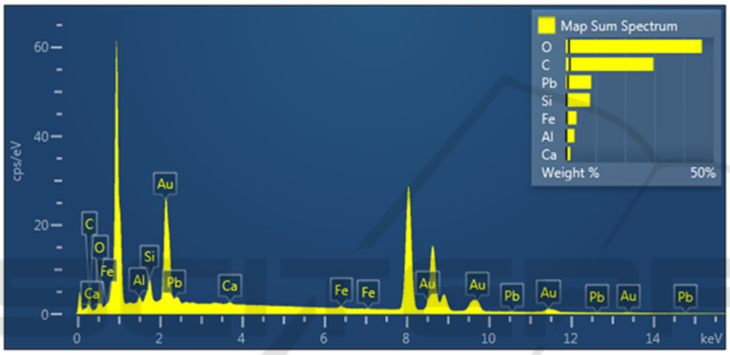
3. Results

3.1. Physicochemical characterization

SEM images of the PM are shown in Figure 1. From this, different particulate materials added to the filter in form of fiber could be observed. Particles with a huge range of sizes could be identified in all micrographs, from the images particles between 100 nm and 3 µm could be seen. In most of the cases amorphous matter is observed from the micrographics.

EDS analysis is one easy and powerful tool in the chemical composition determination of different materials, Figure 2 show the EDS spectrum and tabulated results obtained from the sample (Wt is the weight), respectively.

From the EDS results, carbon (C), oxygen (O), silicon (Si) and lead (Pb), are the most abundant elements present in all samples, probably all metals are in the form of oxides. Of these components silicon and oxygen are associated with the filter material and carbonaceous materials have already been widely studied. Reason why Pb has been chosen to conduct in silico studies of the effect of this element on cardiac electrical activity.



Element	Wt%	Wt% Sigma
C	29.61	1.24
O	46.03	0.95
Al	2.81	0.13
Si	8.09	0.21
Ca	1.46	0.15
Fe	3.51	0.27
Pb	8.50	0.65
Total	100	

Figure 2. EDS spectrum and compositional results.

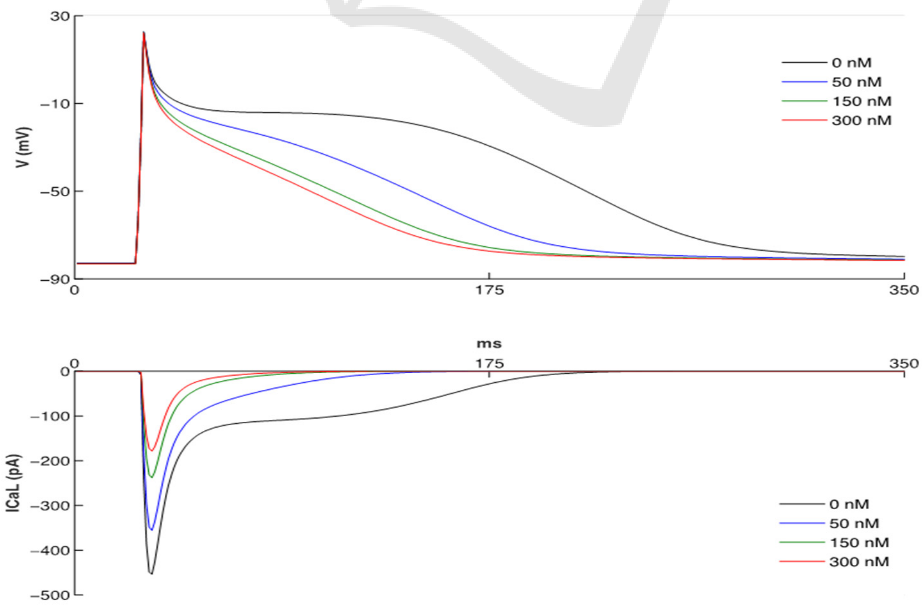


Figure 3. Pb effect on action potential (top) and I_{CaL} (botton) at different concentration.

3.2. Pb effect on cardiac electrical activity

According to a study in ventricular myocytes, Pb affects the cardiac electrical activity by blocking the L-type calcium channels (I_{CaL}) [21]. Additionally, based on the results of the PM characterization where Pb appears as one of the main components, we simulated the Pb effect on cardiac electrical activity. Figure 3 shows the effects of different Pb concentrations on I_{CaL} and action potential, under normal electrophysiological conditions. It can be observed that I_{CaL} without Pb effect shows a peak of -456 pA, the current remains active during the plateau phase of action potential. The APD_{90} has a value of 291 ms under control conditions. First we applied different Pb concentrations. As the Pb concentration increases, I_{CaL} downregulation is observed, which causes an APD shortening and loss of plateau phase. When the highest Pb concentration was applied (300 nM), the I_{CaL} peak decreased 60% (-181 pA) and the APD_{90} reached a value of 152 ms, which indicates a decrease of 48%. The RMP did not show significant changes (-83 mV approximately).

4. Discussion

A total of two PM filters from an environmental monitoring station in a residential area of Medellin were analyzed. The results of the PM characterization showed high concentrations of C, O, Si and Pb, where the C and Si are part of the filter material. Pb was chosen to study its effect on cardiac electrical activity by simulation, because carbonaceous materials have already been widely studied. These results are in agreement with previously reported results of PM. A study in the city of Bogotá [16] showed that the higher metal contents in the PM were mainly related to lead (Pb) and iron (Fe). A study in the city of Medellin also showed the Pb as an important component of the PM [22].

After simulating the effect of Pb on cardiac activity based on experimental studies, our results showed that Pb blocks the I_{CaL} in a fraction greater as the concentration increases, prolonging its action in time, which results in an APD shortening as was demonstrated experimentally [21]. This analysis is consistent with an experimental study in ventricle myocytes of rats [21], where the Pb blocked the L-type calcium channels. A study in ventricular myocardium of rats suggests that acute Pb administration reduces the myocardial contractility by reducing sarcolemmal calcium influx and the myosin ATPase activity [23]. In neurons has been observed that Pb may alter the bioelectrical properties through blocking high voltage activated Ca^{2+} currents, particularly L-type [24], and differentially blocks the cloned T-type calcium channels [25]. There are not in silico studies of Pb effect on human action potential.

In silico studies may contribute to a better understanding of the mechanisms by which air pollutants have unhealthy effects on cardiac tissue, promoting cardiac diseases as arrhythmias.

5. Conclusions

Physicochemical characterization of air particulate matter in Medellin city, evidence the obtaining of particulate material in a huge range of sizes from 100 nm until 3 um and different morphologies. Carbon, oxygen, silicon and lead, were found as the major elements present in the PM. Lead was found as one of the major elements in the particulate matter. Pb was chosen to study its effect on cardiac electrical activity. Our results show pro-arrhythmic effect of Pb on expressed through shortening of APD, during normal electrophysiological conditions. In silico studies may help to better understand the mechanism of how air pollution could trigger cardiac diseases.

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