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On Modeling for Prediction of the Effects of Carbon-Monoxide on Humans Operating under Continuous and Periodic Exposures

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ABSTRACT

The advancements in technological innovations and the utilizations of some technological products or research outcomes have adversely affected the environment and in consequence, continuously pose serious threats to future survival of humans. To counter these assaults of the resultant environmental pollution and the threats of further degradation of the environment, the basic recommended approach for predicting the impact of the pollution and for the determination of the risk assessment strategies is through the use of mathematical models. In the list of various pollutants, carbon monoxide has been established as a major pollutant that seriously affects human health by converting the Oxyhemoglobin (O_2Hb) in the blood to carboxyhemoglobin (COHb). Therefore, this paper presents mathematical models for the computations of carbon-monoxide and carboxyhemoglobin in the blood for the cases of humans under environmental and occupational exposures i.e. operating under continuous and periodic exposures to the pollutant. The developed models are solved analytically using Laplace transforms. The computed results show good agreement with the established experimental results. Using the percentage of COHb in the blood as a good index of health effects of carbon monoxide (CO) on humans, the computed COHb from the developed models is used to predict the effects of CO on human health. On the validation of the developed models, the computed results show good agreement with experimental results. Also, effects of the models parameters on the amount of COHb in the blood. This work will assist in evaluating the technological injuries, effectively controlling our pollutants emissions and also as a tool for designing and developing better equipment and engines with lower or zero emissions.

Key words: Mathematical Models; Carbon-Monoxide; Carboxyhemoglobin; Human Health Effects

INTRODUCTION

The deterioration of environmental quality began with the congregating of mankind into groups, such as, hamlets, villages etc. and became serious problem since the industrial revolution. In the second half of the twentieth century, under the ever-increasing impacts of the exponentially growing population and of the industrializing society, environmental contamination of the air, water, soil and food steadily became a threat to the very survival of the human race [1-56]. Understandably, many signified industrial and governmental communities have recently committed large resources of money and human power to the problem of environmental pollution and pollution abatement by effective control measures focusing on achieving air quality standard in accordance with the Clean Air Act of 1967 [57]. However, in order to resolve the problems, one must predict the ambient air concentrations that will result from any planned set of emissions. According to El-Harbawi *et al.* [58], mathematical models are extremely useful tools to predict the impacts of chemical process accidents. Developing such models will drastically reduce the cost and the task associated with experimentations, as an alternative way of determining the effects of the pollutants.

Following the increase in vehicular traffic and rapid industrialization, carbon-monoxide (CO) is considered as a common atmospheric pollutant that directly affects human health (Singh *et al.*, [59]). Carbon monoxide is colourless, odourless and tasteless. It gives no indication of its presence, which makes it very dangerous and hence, a silent killer. The formations of CO are witnessed in car engines, faulty gas cookers, water heaters and fires, usage of hydrocarbon-burning appliance a room with inadequate ventilation, burning of fuels containing carbon, e. g. gas, wood, oil or paraffin. It is present in cigarette smoke. The adverse effects of this pollutant have aroused the interests of many researchers to study the emission and the degree of the effects of the pollutant on human health. In earlier works, Coburn *et al.* [60] and Latiies [61] pointed out the effects of relatively small CO exposures, which are normally

found in urban, industrial and household air while in the recent times, Gallagher and Mason [62] presented a study on carbon monoxide poisoning in two workers using an LPG forklift truck within a cold store. As part of their findings, the clinical assessment with mathematical exposure modelling may lead to successful retrospective diagnosis of CO poisoning and identify putative work activities. Moreover, the CO poisoning should be suspected whenever internal combustion engines are used within buildings and workers complain of relevant symptoms. From the biological investigations, correlation was found to exist between environmental pollution and human health. Hence conclusions were reached that several disease processes involve factors of environmental pollution, such as, the direct effects of pollution on lungs involving lung diseases and indirect effects on all parts of the body. The adverse effects of air pollution on health were further corroborated by Ren and Tong [63]. Providing solutions or finding a way to abate the problems if not totally eliminated, has been the ultimate purpose of most concerned researchers. One way of establishing a solution is to developed mathematical models for the computations of CO and COHb in the blood. As pointed out by El-Harbawi *et al.* [57], the development of mathematical models for the computation of percentage COHb in due blood has been used to predict the impacts of the pollutant on human health. Since, hemoglobin has as much as 200 times affinity for CO as readily as Oxygen, when inhaled, it binds reversibly with blood hemoglobin to form carboxyhemoglobin, impairing the oxygen-transport capacity of the blood, as well as the oxygen's release to body tissues. Therefore, the percentage of COHb in the blood has been considered as a good index of health effects of CO on humans [64]. Therefore, Forbes *et al*. [65] proposed the formulae to compute COHb level in the blood as a function of exposure time by measuring the rate of CO uptake by humans under a wide range of conditions. Also, Forster *et al.* [66] derived an equation containing 14 parameters to predict the COHb level in the blood while Coburn *et al.* [60] later developed a model for the relationship between blood COHb, rate of CO production and the respiratory CO exchange. In the model, a constant concentration of O_2Hb in the blood was assumed based on the linearized nature of the developed equation. However, Peterson and Stewart [67] pointed out that the constant value of O_2Hb in the Coburn *et al's* equation (CFK equation) led to a significant error in the computation of blood COHb. Therefore, they proposed an iterative procedure for accounting the variation of O_2Hb in the CFK equation. The nonlinear CFK equation was solved numerically by Bernard and Duker [68] equation using the fourth order Runge Kutta method while in the same year, Tyuma *et al.* [69] obtained an analytical solution of the CFK equation while assuming that hemoglobin is always saturated with O_2 or CO or both. Also, Collier and Goldsmith [70] adopted the method proposed by Roughton and Darling [71] to solve the CFK equation by taking into consideration the reduced hemoglobin. Although the CFK equation was developed for the prediction of the concentration of CO in the body, it has been widely used to predict blood COHb under different CO exposures (Weir and Viano [72]; Marcus [73]; Tikuisis *et al*. [74], Wallace *et al.* [75]). More than three decades ago, Ott and Mage [76] and Venkatram and Louch [77] proposed linear models for the computation of the percentage COHb in the blood. Most of the above reviewed developed models are based on empirical laws and which are do not appear to be derived from the basic physical principles. In developing the mathematical models that are based on physical principles, a great deal of complexities arises both in the solution and the involving parameters. This can be established in the works of Singh *et al*. [59] and Sobamowo [78] where systems of partial differential equations are developed and solved using finite difference implicit scheme for the computations of carbon monoxide and carboxyhemoglobin in the blood. It should therefore be noted that, the quest for the development of simple mathematical models for the computation of CO and COHb in the blood has been on. Consequently, in this work, simple mathematical models are developed to predict the effects of the CO on human health. The model developed are functions of exposure time and the ambient pollutant concentration. This will serve as a way of evaluating our technological injuries, effectively controlling our pollutants emissions and also as a tool for designing and developing better equipments and engines with lower emissions.

MATERIALS AND METHODS

Theoretical Background

Carbon monoxide absorption is mainly controlled by physical processes, and occurs in two primary steps. In the first step, the absorption is through the alveolar wall into the alveolar interstitium (this can be affected by the mechanical action of the respiratory system as well as changes to the respiratory tract). From there, the compound moves with a concentration gradient into the red blood cell, similar to molecular oxygen. In both cases, diffusion is established that very rapid, and is driven primarily by the partial pressure differential of carbon monoxide. However, other factors, including oxyhemoglobin and carboxyhemoglobin levels, ventilatory pattern, oxygen consumption, blood flow, and functional residual capacity may affect the rate at which inhaled carbon monoxide enters the blood [66].

The effects of various pollutants on human health are shown in Fig. 1 below. In the pool of these health-damaging pollutants, an air pollutant called carbon monoxide is considered as a common pollutant that directly affects human health as it also produces change in human physiology. Considering the source of this pollutant, it is actually a product of incomplete combustion of hydrocarbon-based fuel, which becomes toxic when inhaled by man due to the strong affinity of hemoglobin (Hb), the oxygen carrier of the blood. Since, the hemoglobin has as much as 200 times affinity for CO as readily as Oxygen, when inhaled, it binds reversibly with blood hemoglobin to form carboxyhemoglobin, impairing the oxygen-transport capacity of the blood, as well as the oxygen's release to body tissues, causing loss of consciousness, fatal asphyxiation, brain damage and all other kinds of health effects as shown in Table 1 below. Death occurs in human exposed to concentration of around 1000 ppm, corresponding to blood levels of 60% COHb. Reasonably, correlations have been found between daily mortality levels and CO. In addition, heart function has been shown to be altered by elevated COHb, as evidenced by the electrocardiograms of exposed healthy adults.

Table 1: Effects of Carboxyhemoglobin (COHb) in the blood on Human health [79]

. **Percentage of carboxyhemoglobin (COHb) in the blood**	**Effect**
0.3-0.7	*Physiologic norm for nonsmokers*
2.5-3.0	*Cardiac function decrements in impaired individuals, blood flow alterations; and, after extended exposure, changes in red blood cell concentration.*
4.0-6.0	*Visual impairments, vigilance decrements, reduced maximal work capacity*
3.0-8.0	*Routine values in smokers. Smokers develop more red blood cells than nonsmokers to compensate for this, as do people who live at high elevations, to compensate for the lower atmospheric pressure.*
10.0-20.0	*Slight headache, lassi-breathlessness from exertion, dilation of blood cells in the skin, abnormal vision, potential damage to foetuses.*
20.0-30.0	*Severe headaches, abnormal manual dexterity.*
30.0-40.0	*Weak muscles, nausea, vomiting, dimness of vision, severe headaches, irritability, and impaired judgment.*
50.0-60.0	*Fainting, convulsions, coma*
60.0-70.0	*Coma, depressed cardiac activity and respiration, sometimes fatal*
>70.0	*Fatal*

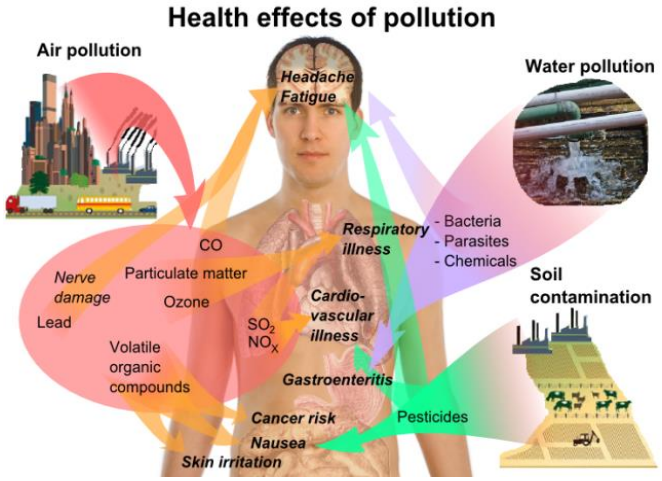

Fig. 1: Overview of main health effects on humans from some common types of pollution [80]

Development of the Predictive Mathematical Models

In this section, mathematical are developed for predicting the effects of pollutant on human health.

Oxygen- Hemoglobin Binding Kinetics

Primarily, oxygen is transported through blood by binding to hemoglobin (a tetrameric molecule

containing four globin chains each with its own heme group). This is because, oxygen is sparingly soluble in aqueous solutions [80]. It should be noted that Hemoglobin contains four heme groups each capable of reversibly binding to one oxygen molecule [80-83].Oxygen binding to any of these sites causes a conformational change in the protein, facilitating binding to each of the other sites. Due to the conformational change that occurs in hemoglobin after oxygen binds to it, the kinetics describing the binding are complex. However, the initial binding of oxygen and hemoglobin can be modeled as a bimolecular reaction [84]:

$$O_2 + Hb \underset{k'_{-1}}{\overset{k_1}{\rightleftarrows}} HbO_2 \quad (1)$$

The rate expression for the formation of the oxygenated hemoglobin is

$$\frac{dC_{HbO_2}}{dt} = k'_1 C_{O_2} C_{Hb} - k'_{-1} C_{HbO_2} \quad (2)$$

where C_{O_2} is the concentration of dissolved oxygen in the solution and is given as

$$C_{O_2} = HP_{O_2}$$

Where H is the Bunsen solubility coefficient, and P_{O_2} is the partial pressure of oxygen present in the lung is approximately

The corresponding rate coefficients for oxygen biding to human hemoglobin at 37^{oC} and pH 7.1 are:

$$k'_1 = 3.5\times10^6 M^{-1}s^{-1} \text{ and } \quad k'_{-1} = 44 s^{-1}$$

A better approach that could be used in transport model is to represent k'_1 as a function of saturation [85]

$$k'_1 = \frac{k'_{-1}}{C_{50}}\left(\frac{S}{1-S}\right)^{\left(1-\frac{1}{n}\right)} \quad (3)$$

Where:

$$S = \frac{\left(\frac{P}{P_{50}}\right)^n}{1+\left(\frac{P}{P_{50}}\right)^n}$$

$C_{50} = \alpha P_{50}$, $n=2.7$, $P_{50}=26$ mmHg (3465.5 Pa)

k'_1 can be written in terms of partial pressure of oxygen as:

$$k'_1 = \frac{k'_{-1}}{\alpha P}\left(\frac{P}{P_{50}}\right)^n \quad (4)$$

The partial pressure of oxygen present in the lung is approximately 13,328.9 Pa (or 100 mm Hg), and the concentration of oxygen in blood plasma is 1.34 ×10^{-4} M. The solubility coefficient for oxygen in red blood cells at saturated temperature and pressure is 1.125×10^{-11} mole cm^{-3} Pa^{-1}. The molecular weight of hemoglobin is 64,500 [84].

A more detailed model could be developed by considering the sequential oxygenation of the four heme groups [84].

$$O_2 + Hb_4(O_2)_{i-1} \underset{k_{-i}}{\overset{k_i}{\rightleftarrows}} Hb(O_2)_i \qquad i = 1, 2, 3, 4 \quad (5)$$

In such a detailed model, the rate expression for the formation of the oxygenated hemoglobin is

$$\frac{dC_{Hb_4(O_2)_i}}{dt} = k_1 C_{O_2} C_{Hb_4(O_2)_{i-1}} - k_{-i} C_{Hb_4(O_2)_i} \quad (6)$$

In the above model, i-1=10 refers to deoxygenated hemoglobin. The rate coefficients for human hemoglobin at 21.5^{oC} and pH 7.0 are

$$k_1 = 17.7\times10^4 M^{-1}s^{-1}, k_{-1} = 1990 s^{-1}$$

$$, k_2 = 33.2\times10^4 M^{-1}s^{-1}, k_{-2} = 0.158 s^{-1},$$

$$k_3 = 48.9\times10^4 M^{-1}s^{-1}, k_{-3} = 0.539 s^{-1},$$

$$k_4 = 33.0\times10^4 M^{-1}s^{-1}, k_{-4} = 0.50 s^{-1}.$$

When oxygen is bound to all four heme groups, the concentration of oxygen bound to hemoglobin per total blood volume is 9.2 ×10^{-3} M.

Carbon Monoxide- Hemoglobin Binding Kinetics

Carbon monoxide binds to hemoglobin at the same sites as oxygen, but approximately 200 times more tightly [82]. Normally, oxygen would bind to hemoglobin in the lungs and be released in areas with low oxygen partial pressure (e.g. active muscles). When carbon monoxide binds to hemoglobin, it cannot be released as easily as oxygen [83]. The slow release rate of carbon monoxide causes an accumulation of CO-bound hemoglobin molecules as exposure to carbon monoxide continues. Because of this, fewer hemoglobin particles are available to bind and deliver oxygen, thus causing the gradual suffocation associated with carbon monoxide poisoning [82].

Carbon monoxide is removed from the body by exhalation following dissociation from heme. Although, the reversible process is slow, COHb releases carbon monoxide slowly. Therefore, one

could develop the rate expression for the formation of the carboxyhemoglobin as:

$$CO + Hb \underset{l_1}{\overset{l_1'}{\rightleftarrows}} COHb \quad (7)$$

Therefore, one could write the rate expression for the formation of the carboxyhemoglobin as

$$\frac{dC_{COHb}}{dt} = l_1' C_{CO} C_{Hb} - l_1 C_{COHb} \quad (8)$$

The prime sign indicates an association velocity constant and its absence indicates a dissociation velocity constant. It should be noted that both the initial formation and the decline of COHb formation and the decline of COHb levels are best modeled by second-order functions, with an initial rapid decay followed by a more gradual second phase [83].

Since, carbon monoxide binds to hemoglobin at the same sites as oxygen, we could also develop a more detailed kinetic model by considering the sequential binding of carbon monoxide to the four heme groups.

$$CO + (CO)_{i-1} Hb_4 \underset{l_i}{\overset{l_i'}{\rightleftarrows}} (CO)_i Hb \qquad i = 1, 2, 3, 4 \quad (9)$$

In such a detailed model, the rate expression for the formation of the oxygenated hemoglobin is

$$\frac{dC_{(CO)_i Hb_4}}{dt} = l_i' C_{CO} C_{(CO)_{i-1} Hb_4} - l_i C_{(CO)_i Hb_4} \quad (10)$$

The simple association and dissociation velocity constants *l'* and *l* help in describing the overall reaction rate. In the four subunits, each step has its own combination and dissociation velocity constants.

Carbon Monoxide Absorption Kinetics

As reported by Coburn and Forman [81], the blood COHb in the body is determined by the exchange of CO between the pulmonary capillary blood and the ambient air, endogenerous production of CO, dilution of CO in the body tissue and metabolic consumption of CO, while the ambient air is transported to alveoli by ventilation. The blood then absorbs the CO from alveoli when it passes through the pulmonary capillaries.

In this section, simple mathematical models developed for the computation of percentage COHb in the human blood for the subject exposed to permanent constant flux of atmospheric pollution.

Model assumptions

The model is based on the following assumptions:

i. The diffusion coefficient of hemoglobin and COHb are assumed to be the same. This is because the molecular mass of CO is much smaller compared to that of hemoglobin.

ii. The diffusion rate is very fast with a constant speed.

iii. The volume of blood remained constant during the diffusion process.

iv. The blood is considered to be fully saturated with O_2 in the pulmonary capillary because it is almost fully saturated during most of the time.

Applying the principle of continuity,

$$V \frac{dC_{CO}}{dt} = F_1 b C_a - \left(F_2 b + F_3 k \right) C_{CO}. \quad (11)$$

The above Eq. (1) can be written as

$$V \frac{dC_{CO}}{dt} + \left(F_2 b + F_3 k \right) C_{CO} = F_1 \, b \, C_a. \quad (12)$$

On solving the differential Equ. (12) using Laplace transform, one arrives at

$$C_{CO} = \left[\frac{F_1 b C_a}{F_2 b + F_3 k} \left(1 - e^{-\frac{(F_2 b + F_3 k)t}{V_b}} \right) + C_o e^{-\frac{(F_2 b + F_3 k)t}{V_b}} \right]. \quad (13)$$

It should be noted that:

$$as \; t \to \infty, \; F_1 b \to F_2 b + F_3 k, C_{CO} \to C_a.$$

For the subject with a periodic or an occupational exposure to constant atmospheric pollutant at regular intervals of T, this is captured by Equ. (14) as:

$$C_{CO} = \left[\frac{F_1 b C_a}{F_2 b + F_3 k} \left(e^{\frac{(F_2 b + F_3 k)T}{V_b}} - 1 \right) \times e^{-\frac{F_2 b + F_3 k}{V_b}(t-(n-2)T)} + C_o \, e^{-\left(\frac{(F_2 b + F_3 k)t}{V_b}\right)} \sum_{n=1}^{N} e^{-\frac{F_1 b + F_2 k}{V_b}(n-1)T} \right] \quad (14)$$

From the International Committee for Standardization in Haemology, we have

$$\% \, COHb = \frac{C_{CO}}{Hb \times 1.398}. \quad (15)$$

The expression for a subject exposed to continuous constant flux of the pollutant for a time, *t*, is

$$\%\ COHb = \frac{1}{Hb \times 1.398}\left[\frac{F_1 b c_a}{F_2 b F_3 k}\left(1-e^{-\left(\frac{(F_2 b+F_3 k)t}{v}\right)}\right) + C_0\, e^{-\left(\frac{(F_2 b+F_3 k)t}{v}\right)}\right]\times 100 \quad (16)$$

Similarly, for the subject with a periodic or an occupational exposure to the constant atmospheric pollutant at regular intervals of time, T, Eq. (17) was developed.

$$\%CoHb = \frac{1}{Hb\times 1.398}\left[\frac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{V_b}}-1\right) \times e^{-\frac{F_2 b+F_3 k}{V_b}(t-(n-2)T)} + C_o\, e^{-\left(\frac{(F_2 b+F_3 k)t}{V_b}\right)} \times \sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{V_b}(n-1)T}\right]\times 100. \quad (17)$$

With the aim of simplifying the model for ease of computation, some factors are developed for the conversion of CO content in the blood to percentage COHb within the range of 1- 4 hours of exposure to atmospheric CO. These conversion factors as shown in Table 2 can be used instead of Eq. (15). Thus, Eq. (16) and (17) could be written as Equs. (18) and (19).

For a subject exposed to continuous constant flux of the pollutant for a time, t, we have

$$\%\ CoHb = \alpha\left[\frac{F_1 b c_a}{F_2 b F_3 k}\left(1-e^{-\left(\frac{(F_2 b+F_3 k)t}{V_b}\right)}\right) + C_o e^{-\left(\frac{(F_2 b+F_3 k)t}{V_B}\right)}\right]. \quad (18)$$

And for an occupational exposure to the constant atmospheric pollutant at regular intervals of time, T,

$$\%CoHb = \alpha\left[\frac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{V_b}}-1\right) \times e^{-\frac{F_2 b+F_3 k}{V_b}(t-(n-2)T)} + C_o\, e^{-\left(\frac{(F_2 b+F_3 k)t}{V_b}\right)} \times \sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{V_b}(n-1)T}\right]. \quad (19)$$

Osgood [86] presented the variation of volume of blood as a function of sex and body weight of the subject as:

$$V_b = \frac{m_b}{13} \text{ for male} \quad (20a)$$

$$V_b = \frac{m_b}{15} \text{ for female} \quad (20b)$$

while,

$$V_b = \begin{cases} 0.071 m_b & 15\ years \\ 0.075 m_b & 10\ years \\ 0.080 m_b & 1-6\ years \end{cases} \quad (20c)$$

while for male and female above the age of 15 years exposed to a continuous constant flux of pollutant for a time, *t*,

$$\%CoHb = \begin{cases} \alpha\left[\frac{F_1 b c_a}{F_2 b F_3 k}\left(1-e^{-\left(\frac{13(F_2 b+F_3 k)t}{m_b}\right)}\right) + C_o e^{-\left(\frac{(13F_2 b+F_3 k)t}{m_b}\right)}\right] & \text{male} > 15\ years \\ \alpha\left[\frac{F_1 b c_a}{F_2 b F_3 k}\left(1-e^{-\left(\frac{15(F_2 b+F_3 k)t}{m_b}\right)}\right) + C_o e^{-\left(\frac{15(F_2 b+F_3 k)t}{m_b}\right)}\right] & \text{female} > 15\ years \end{cases} \quad (21)$$

while for male and female below the age of 15 years exposed to a continuous constant flux of pollutant for a time, t,

$$\%CoHb = \begin{cases} \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(1-e^{\frac{(F_2 b+F_3 k)T}{0.071 m_b}}\right)\right] \\ \quad +C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.071 m_b}} \\ 15\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(1-e^{\frac{(F_2 b+F_3 k)T}{0.075 m_b}}\right)\right] \\ \quad +C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.075 m_b}} \\ 10\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(1-e^{\frac{(F_2 b+F_3 k)T}{0.080 m_b}}\right)\right] \\ \quad +C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.080 m_b}} \\ 1-6\,years \end{cases} \quad (22)$$

While for male and female above the age of 15 years with a periodic or occupational exposure to the constant atmospheric pollutant at regular intervals of time, T,

$$\%CoHb = \begin{cases} \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{13(F_2 b+F_3 k)T}{m_b}}-1\right)\right. \\ \quad \times e^{-\frac{13(F_2 b+F_3 k)}{m_b}(t-(n-2)T)} \\ \quad \left.+C_o e^{-(\frac{13(F_2 b+F_3 k)t)}{m_b}}\sum_{n=1}^{N} e^{\frac{13(F_2 b+F_2 k)}{m_b}(n-1)T}\right] \\ \text{male } > 15\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{15(F_2 b+F_3 k)T}{m_b}}-1\right)\right. \\ \quad \times e^{-\frac{15(F_2 b+F_3 k)}{m_b}(t-(n-2)T)} \\ \quad \left.+C_o e^{-(\frac{15(F_2 b+F_3 k)t)}{m_b}}\sum_{n=1}^{N} e^{-\frac{15(F_2 b+F_2 k)}{m_b}n-1)T}\right] \\ \text{female } > 15\,years \end{cases} \quad (23)$$

and for male and female below the age of 15 years with a periodic exposure to the constant atmospheric pollutant at regular intervals of time, T,

$$\%CoHb = \begin{cases} \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.071 m_b}}-1\right)e^{-\frac{F_2 b+F_3 k}{0.071 m_b}(t-(n-2)T)}\right. \\ \quad \left.+C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.071 m_b}}\sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.071 m_b}(n-1)T}\right] \\ 15\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.075 m_b}}-1\right)e^{-\frac{F_2 b+F_3 k}{0.075 m_b}(t-(n-2)T)}\right. \\ \quad \left.+C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.075 m_b}}\sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.075 m_b}(n-1)T}\right] \\ 10\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.080 m_b}}-1\right)e^{-\frac{F_2 b+F_3 k}{0.080 m_b}(t-(n-2)T)}\right. \\ \quad \left.+C_o e^{-(\frac{(F_2 b+F_3 k)t)}{0.080 m_b}}\sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.080 m_b}(n-1)T}\right] \\ 1-6\,years \end{cases} \quad (24)$$

Therefore, for male and female above the age of 15 years, one arrives at

$$\%CoHb = \begin{cases} \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{13(F_2 b+F_3 k)T}{m_b}}-1\right)\right. \\ \quad \times e^{-\frac{13(F_2 b+F_3 k)}{m_b}(t-(n-2)T)} \\ \quad \left.+C_o e^{-(\frac{13(F_2 b+F_3 k)t)}{m_b}}\sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.071 m_b}(n-1)T}\right] \\ \text{male } > 15\,years \\ \alpha\left[\dfrac{F_1 b c_a}{F_2 b+F_3 k}\left(e^{\frac{13(F_2 b+F_3 k)T}{m_b}}-1\right)\right. \\ \quad \times e^{-\frac{13(F_2 b+F_3 k)}{m_b}(t-(n-2)T)} \\ \quad \left.+C_o e^{-(\frac{13(F_2 b+F_3 k)t)}{m_b}}\sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.071 m_b}(n-1)T}\right] \\ \text{female } > 15\,years \end{cases} \quad (25)$$

and for children under the age of 15 years

$$\%CoHb = \begin{cases} \alpha\left[\frac{F_1 b c_a}{F_2 b + F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.071 m_b}} - 1\right)e^{-\frac{F_2 b+F_3 k}{0.071 m_b}(t-(n-2)T)} + C_o e^{-\left(\frac{(F_2 b+F_3 k)t}{0.071 m_b}\right)} \sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.071 m_b}(n-1)T}\right] & 15\,years \\ \alpha\left[\frac{F_1 b c_a}{F_2 b + F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.075 m_b}} - 1\right)e^{-\frac{F_2 b+F_3 k}{0.075 m_b}(t-(n-2)T)} + C_o e^{-\left(\frac{(F_2 b+F_3 k)t}{0.075 m_b}\right)} \sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.075 m_b}(n-1)T}\right] & 10\,years \\ \alpha\left[\frac{F_1 b c_a}{F_2 b + F_3 k}\left(e^{\frac{(F_2 b+F_3 k)T}{0.080 m_b}} - 1\right)e^{-\frac{F_2 b+F_3 k}{0.080 m_b}(t-(n-2)T)} + C_o e^{-\left(\frac{(F_2 b+F_3 k)t}{0.080 m_b}\right)} \sum_{n=1}^{N} e^{-\frac{F_1 b+F_2 k}{0.080 m_b}(n-1)T}\right] & 1-6\,years \end{cases} \quad (26)$$

Table 2: Conversion Factors from CO to %COHb.

Time (hr)	Ambient Concentration (ppm)		
	0-50	50-100	100-200
1	0.0475	0.0350	0.0300
2	0.0600	0.0550	0.0525
3	0.0800	0.0750	0.0700
4	0.1000	0.0800	0.0800

RESULTS AND DISCUSSION

The developed mathematical models are simulated using MATLAB and the simulated results are presented as Figs. 2-14. Using the initial percentage of COHb of 0.25% (Singh, [2]), Fig. 2 shows the effects of breathing rate on the percentage concentration of COHb in human subject exposed to a constant concentration flux of 36.9 ppm of ambient CO for a maximum period of 1 hour. From the figure, 1.62 - 1.70 % of the COHb was predicted for breathing rates of 5 – 8L/min.

The subject exposed to a constant concentration flux of 200.8 ppm of ambient CO under the same exposure time depicts an increase in percentage of COHb to a maximum of 5.82 % for the breathing rates 8 L/min (Fig. 3). It could be inferred from the Figures that the percentage of COHb in human subjects increases with increase in the concentration of ambient CO and the breathing rates. Following the Table 1, the subject will experience visual impairments, vigilance decrements and reduced maximal work capacity.

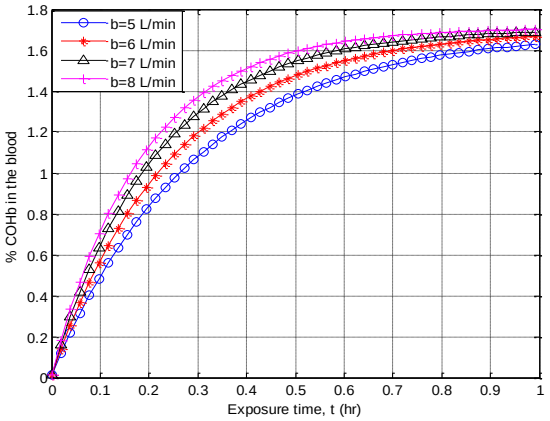

Fig. 2: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 36.9 ppm ambient CO for 1hr

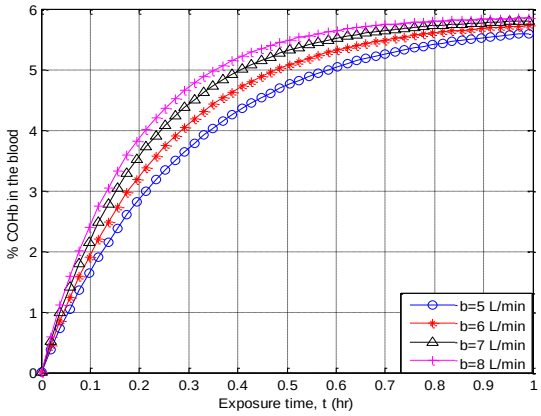

Fig. 3: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 200.8 ppm ambient CO for 1hr

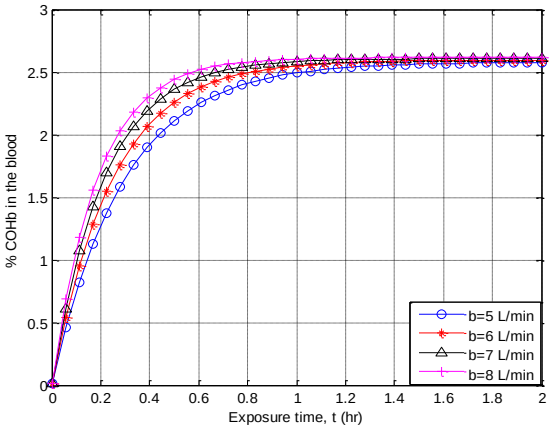

Fig. 4: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 44.7 ppm ambient CO for 2hrs

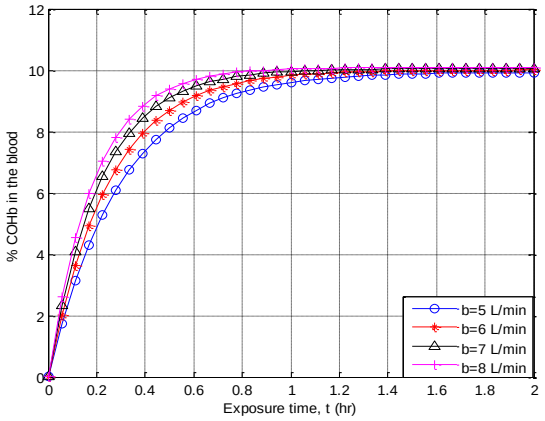

Fig. 5: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 196.9 ppm ambient CO for 2hrs

Figs. 4 and 5 reveals the effects of breathing rates on the percentage of COHb in human subjects exposed to constant concentration fluxes of 44.7 ppm and 196.9 ppm ambient CO respectively, for a period of 2 hours. For these exposures, the percentage of COHb is between 2.5-10.0 %. Therefore, the subject will experience slight headache, lassi-breathlessness from exertion, dilation of blood cells in the skin, abnormal vision, and potential damage to foetuses. Due to its high affinity for hemoglobin, most absorbed carbon monoxide will be found in the blood as carboxyhemoglobin, and therefore present in all tissues of the body. However, carbon monoxide can dissociate from carboxyhemoglobin and enter other tissues with heme-containing enzymes, including the heart and liver.

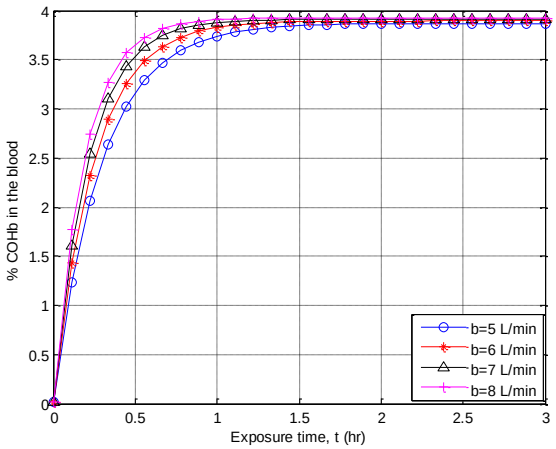

Fig. 6: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 46.0 ppm ambient CO for 3hrs

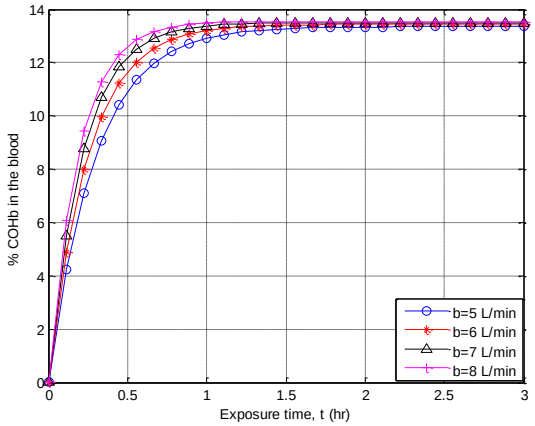

Fig. 7: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 198.4 ppm ambient CO for 3hrs

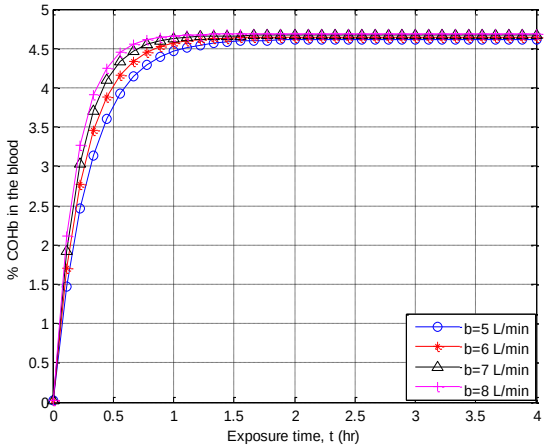

Fig. 8: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 48.0 ppm ambient CO for 4 hrs.

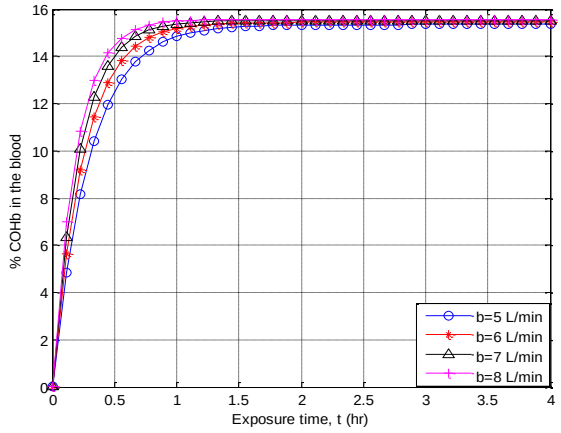

Fig. 9: Effect of breathing rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 199.5 ppm ambient CO for 4 hrs.

The effects of breathing rate on the percentage concentration of carboxyheamoglobin (COHb) in

human subject exposed to a constant concentration fluxes of 46.0, 198.4, 48, 199.5 ppm of ambient CO for periods of 3 and 4 hours are shown in Figs. 6, 7, 8 and 9 while Figs. 10 and 11 depict the effects of blood volume on the percentage concentration of carboxyhemoglobin (COHb) in human subject exposed to a constant concentration fluxes of 36.9 ppm and 200.8 ppm of ambient CO for a maximum period of 1 hour. The variations in blood volume correspond to the variation in the ages and amounts of blood in the subjects. The figures reveal that the percentage of COHb in human subjects increases with increase in the concentration of ambient CO and decreases with the subject's blood volume. The effects of elimination rates and breathed fractions of atmospheric pollutant on the percentage of COHb in human subject exposed to constant concentration flux of 199.5 ppm ambient CO for 1hr are shown in Figs. 12 and 13. The figures describe that the percentage of COHb in human subjects decreases with increase elimination rates and increases with increase in the breathed fractions of atmospheric pollutant.

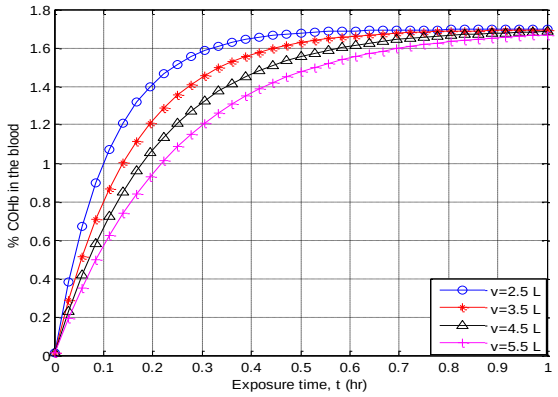

Fig. 10: Effect of volume of blood on the Percentage of COHb in human subjects exposed to constant concentration flux of 36.9 ppm ambient CO for 1hr

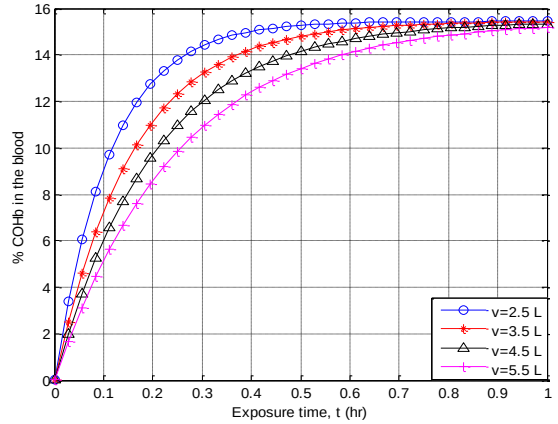

Fig. 11: Effect of volume of blood on the Percentage of COHb in human subjects exposed to constant concentration flux of 200.8 ppm ambient CO for 1hr

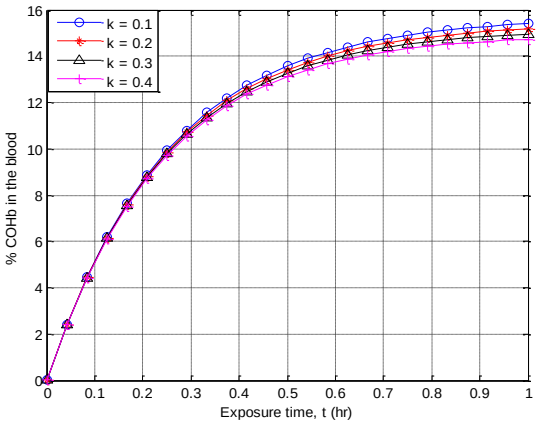

Fig. 12: Effect of elimination rate on the Percentage of COHb in human subjects exposed to constant concentration flux of 199.5 ppm ambient CO for 1hr

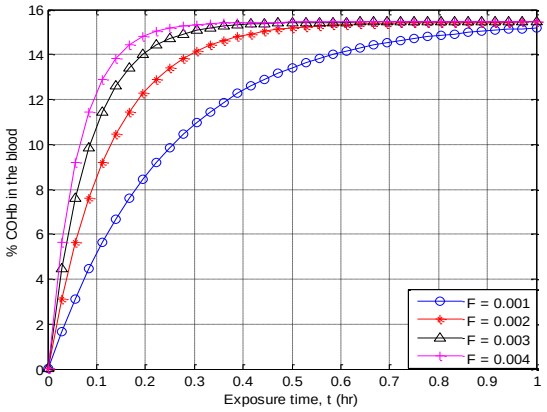

Fig. 13: Effect of breathed fraction of atmospheric pollutant on the Percentage of COHb in human subjects exposed human constant concentration flux of 199.5 ppm ambient CO for 1hr

Since, the percentage of COHb in human subject increases with exposure time and the ambient CO, a subject expose to higher concentrations of CO for a prolong period of time will definitely experience severe headaches, abnormal manual dexterity, weak muscles, nausea, vomiting, dimness of vision, severe headaches, irritability, and impaired judgment, fainting, convulsions, coma, depressed cardiac activity and respiration. As the exposure continues under an increased concentration of ambient CO, the effects of the pollutant will be intensified and severe damage to the subject's health will result. In fact, deaths result when the percentage of COHb in human subject exceeds 70%. Tables 3-6 show the comparison of results and from the results analysis, the computed results in this study show good agreement with experimental results as also shown by Singh *et al.* [59].

Table 3: Comparison and Analysis of Results of Percentage COHb in the blood for 1hr exposure to CO

Ambient concentration (ppm)	Experimental results (Peterson and Stewart)	Singh *et al.* Model	The Present Model
36.9	1.80	1.69	1.72
51.6	2.12	2.00	2.24
87.9	2.90	2.96	2.97
93.5	3.37	3.11	3.16
200.8	5.93	5.93	5.82
Standard Deviation		**1.52**	**1.42**

Table 4: Comparison and Analysis of Results of Percentage COHb in the blood for 2 hrs. exposure to CO

Ambient concentration (ppm)	Experimental results (Peterson and Stewart)	Singh *et al.* Model	The Present Model
25.4	1.50	1.78	1.47
44.7	2.48	2.71	2.60
96.4	5.10	5.20	5.13
196.9	10.08	9.98	10.00
Standard Deviation		**3.18**	**3.28**

Table 5: Comparison and Analysis of Results of Percentage COHb in the blood for 3hrs exposure to CO

Ambient concentration (ppm)	Experimental results (Peterson and Stewart)	Singh *et al*. Model	The Present Model
46.0	3.86	3.54	3.56
51.2	3.75	3.88	3.96
91.9	6.61	6.56	6.67
98.1	7.23	6.97	7.12
99.2	7.02	7.04	7.20
198.4	13.83	13.41	13.44
Standard Deviation		**3.24**	**3.23**

Table 6: Comparison and Analysis of Results of Percentage COHb in the blood for 4 hrs. exposure to CO

Ambient concentration (ppm)	Experimental results (Peterson and Stewart)	Singh *et al*. Model	The Present Model
48.0	5.07	4.33	4.64
98.4	7.34	8.37	7.62
199.5	15.97	16.16	15.44
Standard Deviation		**4.91**	**4.55**

CONCLUSION

In this study, mathematical models for the computations of carbon-monoxide and carboxy-hemoglobin (COHb) in the blood have been developed. The models were used to compute the percentage of COHb in the human subjects. The computed COHb from the developed models was used to predict the effects of carbon-monoxide (CO) on human health. The predicted results show good agreement with those measured experimentally (Peterson and Stewart, [66]) and the models developed by (Singh *et al*. [59]). The variations in the models parameter indicate significant variations in the results. This can be used as a means of controlling the effects of the pollutant on human health.

ETHICAL ISSUES

There is no ethical issue regarding the publication of this paper

CONFLICT OF INTEREST

The author declares that there is no conflict of interest regarding the publication of this paper.

AUTHOR'S CONTRIBUTIONS

The author contributes on the conceptualization of the idea, study design, methodology, writing of the final version of the manuscript etc.

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NOMENCLATURE

b: Rate of breathing or air exchange rate (Lit air/air).

$C_{o:}$ Atmospheric Concentration of carbon monoxide, ppm

C_{CO} : Concentration of carbon monoxide in the blood, ppm

C_{COHb}: Concentration of carboxyheaomoglobin in the blood.

C_o:Initial concentration of carbon monoxide content in the blood, ppm

$F_{1:}$ Fraction of the atmospheric pollutant that is breathed in or taken in through the nose

$F_{2:}$ Fraction of the atmospheric pollutant that is breathed out of the nose

$F_{3:}$ Fraction of the atmospheric pollutant that is removed through the elimination mechanism

K: Net rate or elimination mechanism (Or removal rate) other than air exchange rate (L/min).
N: Number of days of exposure.
V: Volume of blood in human body (L)

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