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Optical method for reduction of carbon monoxide intoxication

S. Mamilov[1], S.Yesman[1], V. Mantareva[2], E. Borisova[3], A. Gisbrecht[3]*

[1] *Institute of Applied Problems of Physics and Biophysics, NAS of Ukraine*
[2]*Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia, Bulgaria*
[3]*Institute of Electronics, Bulgarian Academy of Sciences, Sofia, Bulgaria*

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The efficiency of the laser radiation effect on the carboxyhemoglobin (HbCO) in blood vessels and its dependence on the wavelength and the power of the irradiation are investigated. *In vivo* experimental measurements of the quantum yield of the laser-induced photodissociation of HbCO in cutaneous blood vessels in the visible and near IR spectral range are presented. Arterial HbCO concentration was measured by a method of fingertip pulse oximetry. It is shown that there is a decrease in HbCO concentration in the blood under the influence of the transcutaneous laser irradiation. Three maxima (at 525, 600 and 850 nm) in the spectral range are observed, wherein the decrease in the HbCO concentration exceeds 50 %. Irradiating HbCO at the spectra maximum, we measured a considerably high photodissociation yield of nearly 75%, which ensures high efficiency of photodecomposition of the HbCO in the blood. The obtained results can be used in the clinical phototherapy practice for effective treatment of carbon monoxide intoxication.

Keywords: carboxyhemoglobin, quantum efficiency, photodissociation

INTRODUCTION

Carbon monoxide (CO) is a highly toxic odorless and colorless gas. The mechanism of CO toxicity is connected with its binding to the hemoglobin heme groups. The binding affinity of Hb for CO is about 250 times greater than that for oxygen (O_2), so it reduces the blood oxygen-carrying capacity causing tissue hypoxia [1].

Treatment of CO poisoning is based on restoring gas balance in the blood by providing high oxygen-enriched environment. The rate of dissociation of HbCO is extremely low; the lifetime of CO elimination is about 4-6 hours on air and can be decreased by hyperventilation of the lungs with O_2 for up to 1-2 hours. Hyperbaric oxygen therapy is considered as one of the relatively effective methods of treatment. However, the problem of CO poisoning still remains and monitoring the concentration of HbCO in the blood stream is a very actual problem.

The signs and symptoms of poisoning by CO appear at concentrations higher than 10%, but even a lower concentration of HbCO can cause a health problem particularly for the high-risk group of people. To the latter belong people with cardiovascular and pulmonary diseases, smokers, pregnant and those engaged with certain professions so that the average HbCO for moderate smokers is about 5 % and for heavy smokers may exceed 10% [2]. This range is very important for many clinical applications to estimate the health effect of environment, monitoring neonatal and adult haemolysis, etc., so more effective new methods of treatment need to be developed.

In this report we present a new approach for the treatment of CO poisoning based on photodissociation of HbCO in the blood stream, which allows the recovery of normal oxygen saturation.

Photodissociation of Carboxyhemoglobin

In our previous reports we were continuously developing a model of laser-tissue interaction based on photodissociation of hemoglobin + gas complexes. As a result, the concept of biomedical application of laser-induced photodissociation of oxyhemoglobin has been proposed [3].

Here we extend our concept on carboxyhemoglobin with the aim to develop a new approach in CO poisoning treatment. While the effectiveness of known methods for eliminating the poisoning effect of CO is limited by the lifetime of the HbCO complex, the induced decomposition of HbCO by photodissociation with subsequent saturation of the blood with molecular oxygen can significantly accelerate the removal of CO. The scheme is shown in Fig. 1.

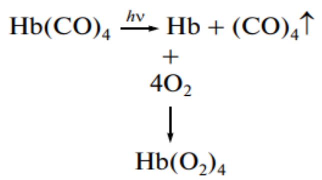

Fig. 1. The scheme of HbCO photodissociation with subsequent saturation of the blood.

* To whom all correspondence should be sent:
E-mail: aigiz@abv.bg

Despite the similarities in the absorption spectra of HbO_2 and HbCO, the significant difference (> 10 times) in the quantum yields of photodissociation makes it possible to obtain selective decomposition of HbCO in the blood stream with a minimum effect on the HbO_2. The suggested method of elimination of CO from blood is based on the optical acting on HbCO in the cutaneous blood vessels through human skin. In this case we must take into account the optical properties of the human skin in order to determine the effective wavelength of the penetrating radiation. This can be achieved by calculating the action spectra of HbCO in the skin.

In our earlier work [4] we presented the calculated absorption spectra of HbCO at different depths (action spectra) and showed that their absorption spectra are transformed by the optical properties of skin into a relatively narrow spectral range.

Since the effect of laser-induced photodissociation of HbCO has been experimentally demonstrated, it is interesting to investigate the spectral dependence of the effect in the irradiation zone. There is practically no information in the literature on the connection between the quantum efficiency of the photodissociation and the wavelength of the irradiating light [5-10]. Also, most studies have been done *in vitro*, so it is reasonable to expect that the *in vivo* photolytic effect will be different from that observed in buffer solutions, considering the different biological environment and specific features of light propagation in biological tissues.

MATERIALS AND METHODS

Determination of HbCO concentration in the blood was performed by a method similar to the method of pulse oximetry which is based on the measurement of light-modulated pulse wave of blood. The values were measured using a pulse 3-wavelengths sensor operating in backscattered light, based on a standard pulse oximetry pair of V97B light emitting diodes (λ= 660 nm and 935 nm) and L-53MGC light emitting diode (λ = 568 nm) and a BPW34 silicon photodiode. Conventional pulse oximeters do not measure the presence of HbCO in arterial blood due to the close spectral characteristics of HbCO and HbO_2 during measurements [8]. Due to our original method of data processing [11] the designed 3-wavelengths measurement system provides a maximum difference in the absorption coefficients of different derivatives of hemoglobin and makes it possible to obtain a reliable measuring of the HbCO level with high accuracy (<0.2%). The system allows continuous photoplethysmographic monitoring, recording and data storage.

The pulse oximetry sensor was placed on the first phalanx of the finger. The light was delivered to the finger from LEDs (or laser diodes) at fifteen wavelengths in the 400–940 nm spectral range. The optical power of every light source was selected to provide an approximately equal number of photons of different wavelengths incident on the irradiated skin area. The corresponding power density of irradiation taking into account the output aperture varied from 50 mW/cm^2 for λ = 405 nm to 125 mW/cm^2 for λ = 940 nm.

The measurements were taken on the fingers of 5 healthy male volunteers including non-smokers and smokers after a 12-hour nonsmoking interval in order to reduce the impact of HbCO on the accuracy of the pulse oximetry. All procedures performed in the study were in accordance with the ethical standards with informed consent obtained from each subject and approval by the institutional review board.

The irradiation beam with a diameter of 4 mm was directed at the lower front of the phalanx, at about 5 mm distance from the measuring sensor, so that direct light did not reach the surface of the photodetector. For each source in each series, 7 to 15 records were made according to the following scheme: 30 s without radiation, 30 s with radiation and 30 s without radiation. For every record the mean values and their change induced by the irradiation were calculated and then averaged over the number of records. In order to eliminate rogue results, only measurements which were within the range between +/- 20% standard deviation from the mean were included in the analysis. All results are given as mean ± (SD). The Student's test for connected sampling was used for the statistical calculations. Statistical results with a value of $p < 0.05$ were viewed as being significant for all volunteers. The evaluation was carried out using the program “Origin 7.5”.

RESULTS

Spectral Dependency

Using described above technique and method we experimentally measured the laser-induced photodissociation of HbCO in cutaneous blood vessels in the visible and near IR spectral range. We determined the parameter ΔHbCO as the difference between the initial values of HbCO before irradiation and the measurable values in the experiment. The initial values of relative HbCO concentration varied from 3.4 % up to 5.9 %.

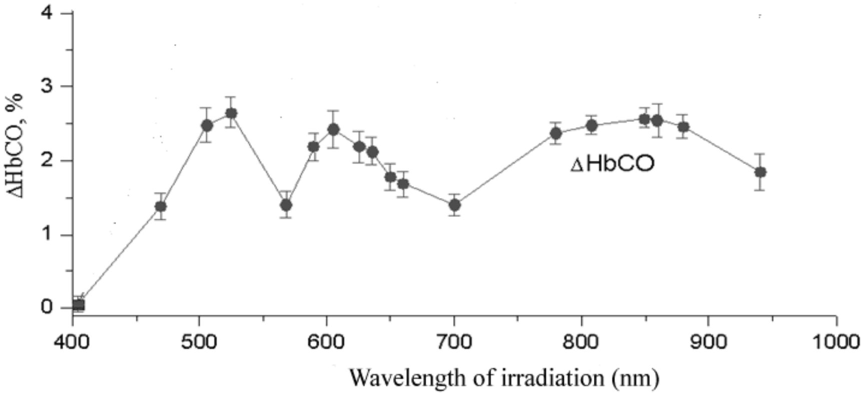

Fig. 2. Change in concentration (%) of HbCO in the arterial blood depending on the irradiation wavelength.

Using statistical analysis of measurement data obtained for all sources of radiation the parameter ΔHbCO was calculated. The results demonstrated that the rate of the HbCO in blood varies under the influence of local transcutaneous light irradiation and significantly depends on the radiation wavelength. Three absorption maxima in the spectral range near 530, 600 and 850 nm were revealed (Figure 2). The results obtained correlate well with the characteristics of light propagation in blood-filled tissues. absorption maxima in the spectral range near 530, 600 and 850 nm were revealed (Figure 2). The results obtained correlate well with the characteristics of light propagation in blood-filled tissues. Light at wavelengths below 450 nm is strongly absorbed in superficial skin layers and irradiation in this spectral range has no effect in the described experiment.

The visible light below 580 nm has a small penetration depth into the skin tissue because of its proximity to the absorption bands of some basic skin chromophores such as hemoglobins and melanin; therefore in real tissue it can cause HbCO photodissociation only in shallow superficial skin layers. Red and especially near IR radiation penetrate much deeper into soft tissues. The experimental results obtained correlate well with the action spectra calculated in [4].

It should be noted that a 2.5% decrease in ΔHbCO occurs at the initial 5%, i.e. irradiation at spectral maxima leads to photolysis of near 50 % of HbCO molecules.

Optical Power Dependency

In this paragraph we present an *in vivo* experimental study of the efficiency of changes in HbCO molecules depending on the laser radiation power and subsequent calculation of the quantum efficiency of light interaction with HbCO in the blood at wavelengths of 525 and 605 nm, which are in the region of the maximum effect in the visible region of the spectrum.

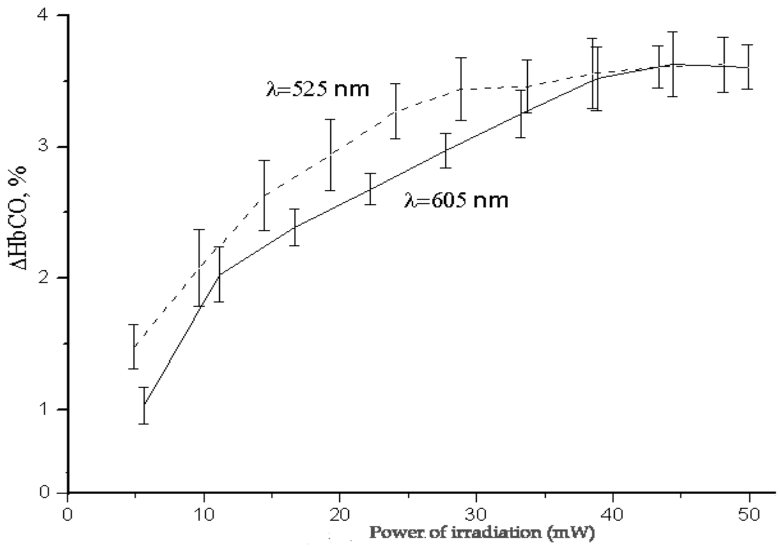

Fig. 3. Change in concentration (%) of HbCO in the arterial blood depending on the power of the irradiation

The mean values of HbCO without irradiation were 4.6 ± 0.33 SD%. Figure 3 shows the change in concentration (%) of HbCO in the arterial blood depending on the irradiation power.

As can be seen from Figure 3, the photo-dissociation process significantly depends on the laser radiation power and reaches saturation at the power above 50 mW (300 mW/cm^2). This means that a further increase in the number of irradiating photons does not lead to an increase in acts of dissociation of molecules in the irradiated blood. We determined the quantum efficiency of light interaction with HbCO as the ratio of relative values of ΔHbCO to the initial values of the HbCO before irradiation, so the obtained maximum values ΔHbCO/HbCO determine their quantum yields of photodissociation. We calculated a photo-dissociation yield of 79% for HbCO at a wavelength of 525 nm and of 76 % at a wavelength of 605 nm. The results obtained correlate well with the quantum yields of photodissociation calculated in [10].

DISCUSSION

In contrast to other studies, this study was carried out under *in vivo* conditions, so it was possible to make statements about the practicability of the effect. It should be noted that the main difference between this study and all other studies previously performed on solutions of Hb complexes is the fact that at *in vivo* condition, due to the blood flow, a constant number of photodissociation objects is provided while at *in vitro* condition the number of molecules that actually undergo photolysis, exponentially decreases.

Thus, we demonstrated that the rate of HbCO in blood varies under the influence of local transcutaneous irradiation and significantly depends on the irradiation wavelength and the irradiation power. It is evident that the observed local decrease in the initial values of HbCO during irradiation is caused by HbCO photodissociation in the blood capillary vessels.

Phototherapy of Carbon Monoxide Poisoning

The results obtained allow us to propose an approach for increasing the effectiveness of carbon monoxide decomposition. It is shown that the significant difference in the quantum yields of photodissociation of hemoglobin complexes makes possible a selective decomposition of HbCO in the blood stream with minimum effect on the HbO_2 component.

The rate of CO photodissociation from the HbCO molecule is extremely high and its quantum yield, which is almost 80%, allows us to expect high efficiency of the proposed approach in clinical applications. Maximum photodissociation of HbCO can be reached in the lungs alveoli or in cutaneous blood vessels by irradiating at wavelengths near 530, 600 and 850 nm, which are in the region of the maximum effect in the visible and IR region of the spectrum. The spectral effectiveness of the photodissociation approximately correlates with the absorption spectrum of HbCO and the transmission spectrum of skin tissue. The required laser power and the treatment time in clinical practice should be determined according to the optical properties of the skin, the depth of penetration and the volume of blood illuminated by laser radiation.

Our approach, based on photodissociation of the blood HbCO, in combination with other existent methods (oxygen hyperventilation, hyperbaric oxygen therapy) significantly increases the efficiency of CO poisoning treatment. An important conclusion is that there is a possibility of laser-induced reduction of HbCO in the blood and thus a recovery of the oxygen-transport function of the blood. The distinctive feature of this technology is its selectivity and local action.

The results of this study cannot identify any immediate effect of the radiation on the HbCO decomposition in tissue *in vivo*. It would be reasonable if further studies on the immediate effects would take into account additional parameters, which along with the observed effects, may have a role in clinical practice.

CONCLUSION

A new approach for the treatment of CO poisoning based on the laser-induced photodissociation of HbCO in the arterial blood is proposed. The results show that there is a decrease in the concentration of HbCO in the blood under the influence of transcutaneous laser irradiation. The rates of HbCO concentration in the blood *in vivo* were experimentally measured depending on the radiation wavelength and the irradiation power. The quantum yield of photodissociation is considerably high in the spectral region of maximum effect (up to 80 %), which ensures high efficiency of photodecomposition of the HbCO in the blood. The results obtained can be used in the clinical phototherapy practice for effective treatment of CO poisoning.

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