JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS Vol. 12, No. 9, September 2010, p. 1942 - 1945

Measurement of the modifications of Polidocanol absorption spectra after exposure to NIR laser radiation

A. SMARANDACHE*, M. TRELLES[a], M. L. PASCU
National Institute for Laser, Plasma and Radiation Physics, Laser Department, P.O.Box, MG-36, 077125, Bucharest, Romania
[a]*Instituto Médico Vilafortuny/FUNDACION ANTONI DE GIMBERNAT, Cambrils, Spain*

Polidocanol (commercially available under the name Aetoxisclerol) is one of the medicines used in the treatment of varicose veins diseases. It seems that exposure of tissues impregnated with Polidocanol to Nd:YAG laser radiation at 1.06μm improves the treatment efficiency. Because the commercially available Aetoxisclerol is a mixture of substances, when it is exposed to laser radiation, one should consider the interaction with all the compounds. The absorption spectra in UV-VIS-NIR spectral ranges are measured for Aetoxisclerol. We exposed it at pulsed Nd:YAG laser beam between 2-30 min at known irradiation doses. The possible mechanisms implied in improvement of the efficiency of Polidocanol are discussed.

(Received July 12, 2010; accepted September 15, 2010)

Keywords: Sclerotherapy, Polidocanol, Laser, Optical absorption spectra

1. Introduction

Lower extremity venous insufficiency is common and increases with age. In addition to classical symptoms, it may result in skin changes and venous ulcers. Chronic venous insufficiency has a great impact on patients' health-related quality of life and is associated with considerable health care costs.

The seventh most common chronic vascular disorder, nine times more frequent than arterial diseases is represented by varicose or spider veins in the lower limbs; almost 60% of the adult population of Europe and the USA present this affection [1]. In recent years, a significant, growing number of patients are consulting in order to correct the symptoms originated in this vascular disorder, as well as the aesthetic implications that cause this ailment. Although the main approach in the treatment of small diameter veins, in venulectasias and reticular veins of less than 4 mm in diameter (class I/II and III) is sclerotherapy [2-4], lasers, especially the Nd:YAG laser, have shown interesting possibilities [5-7].

Modern sclerotherapy is performed using sclerosing detergents such as Polidocanol. Sclerotherapy is the targeted elimination of varicose veins less of 4 mm in diameter by injection of a sclerosing substance into the vein lumen. Sclerosing agents cause a chemical irritation of the venous intimate part that produces an inflammation of the endothelial lining of the vessel. Subsequently, a secondary, wall-attached local thrombus is generated and, in long term, the veins will be transformed into a fibrous cord (sclerosis) [8].

According to their potency, sclerosing agents can be classified as major (alcohol, iodine, sodium tetradecyl sulphate), intermediate (sodium salicylate, polidocanol), or minor (chromated glycerine). Polidocanol is a co-surfactant. It contains a hydrophilic and a hydrophobic pole and acts by altering the surface tension at the interface between the endothelial cells and their environment. The hydrophobic pole binds to the cell surface, whereas the hydrophilic portion attracts water into the cell, resulting in a rapid and intense cell hydration [9].

Clinical observations prove that foam sclerotherapy is preferable instead of the use of liquid sclerosing substances [10-13]. Detergent-like compounds such as polidocanol can be transformed into fine-bubbled foam by special techniques such as the Monfreux technique, the Tessari technique and the double-syringe system technique. The Tessari method is now one of the most popular techniques, using 2 ordinary disposable syringes attached to a 3-way stopcock. These home-made foams use atmospheric air, rich in nitrogen, which is a gas of low solubility in bodily fluid, and they have an irregular bubble size and a highly variable internal cohesion [8].

The understanding of the interaction between the Polidocanol and the target veins (tissues) is an important factor in utilizing it in varicose veins deseases. Clinical experimental results prove that the exposure of the tissues impregnated with Polidocanol to laser radiation emitted at 1.06μm improves the efficiency of the treatment [2].

The aim of this work is to perform an extensive study about the optical properties of commercially available Polidocanol (Aetoxisclerol 2%) and about the possible modifications induced at molecular level in this medicine as supplied by the manufacturer, by exposing it at laser radiaton. This paper presents only the results obtained on the liquid form of Polidocanol.

2. Materials and methods

Polidocanol, $C_{14}H_{30}O_2$ (CAS 3055-99-0), is a polyethylene glycol ether of Lauryl alcohol, where the average value of polymer is 9 [14]. The 3D image of the Polidocanol molecule is shown in Fig. 1, where the carbon atoms are in dark grey colour, the hydrogen atoms are light grey and the oxygen atoms are red.

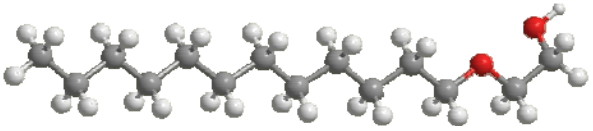

Fig. 1. 3D image of Polidocanol molecule.

Polidocanol, supplied by Kreussler Pharma Gmbh as Atoxisclerol 2% is an intermediate sclerosing substance whose mission is to destroy the endothelial lining of the target vessel; the exposure of the basal layer collagen, induction of vasospasm and ultimately complete vessel fibrosis are its main effects.

In fact, Aetoxisclerol 2% is a mixture of the following substances: Lauromacrogol 400, Sodium hydrogen phosphate**,** Potassium dihydrogen phosphate, Ethyl alcohol and Water. For this reason, when the Aetoxisclerol 2% sollution is exposed to laser beam, one should consider actually the interaction it with all the above mentioned compounds present in the commercial grade substance.

The absorption spectra measurements in spectrophotometer cells of 10 mm optical length are performed on Aetoxisclerol 2% in UV-VIS-NIR using a Perkin Elmer Lambda 980 spectrometer. This spectrometer features a double beam, double monocromator and ratio-recording optical system; the device measuring error is 0.4%.

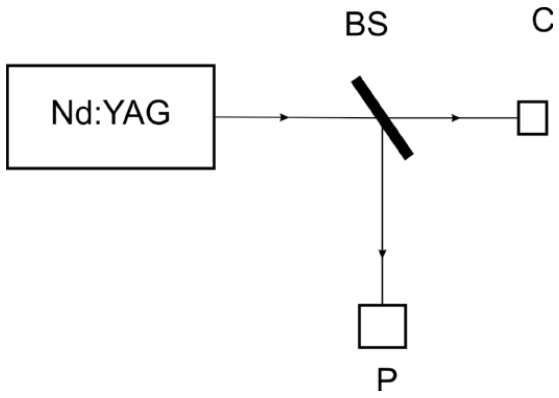

Fig. 2. Experimental set-up for laser irradiation of Polidocanol samples

We exposed Aetoxisclerol 2%, commercialy available at laser beam emitted by a pulsed Nd:YAG laser at 1.06μm, the laser radiation having the following characteristics: pulse repetition rate 10pps, FTW 5ns, beam energy on the sample 1.359mJ. The exposure time was made on samples in bulk, between 2 min and 30 min; the sample (Fig.2) was introduced in a spectrophotometer cell (C) and the corresponding irradiaton dose varied from 3.2 J/cm^2 to respectivelly 45 J/cm^2; 8-10% of the laser radiation was directed through a beam splitter (BS) unto a powermeter (P).

3. Results and disscution

The absorption spectra shown in Fig. 3 and Fig. 4 indicate no significant absorption in the UV-VIS spectral range, and very weak peaks in NIR at 900nm, 1.18 μm, 1.69μm and 1.72μm; they are the result of the superposed absorption of all the compounds included in the commercially available Aetoxisclerol 2%.

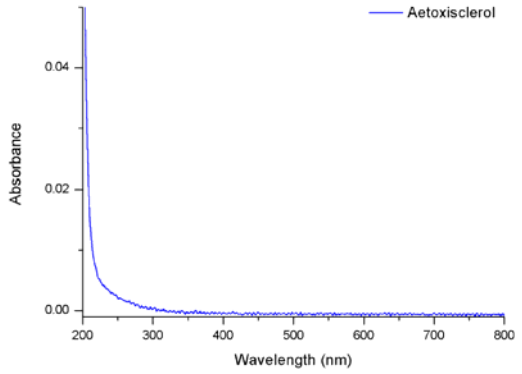

Fig. 3. UV-VIS absorption spectrum of Aetoxisclerol 2%

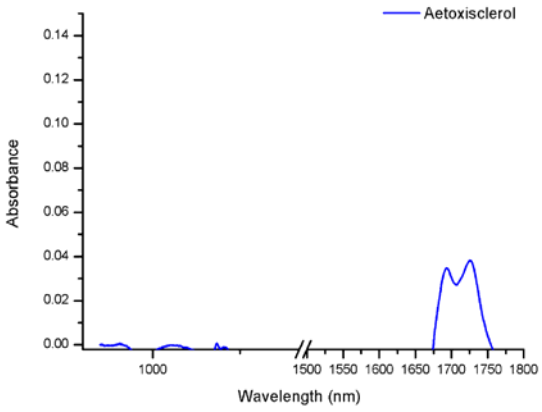

Fig. 4. NIR absorption spectrum of Aetoxisclerol 2%

For instance, the ethyl alcohol, one of the substances included in the commercially available Polidocanol has relatively significant absorption peaks at 900nm, 1μm and 1.2μm as it can be observed in Fig. 5.

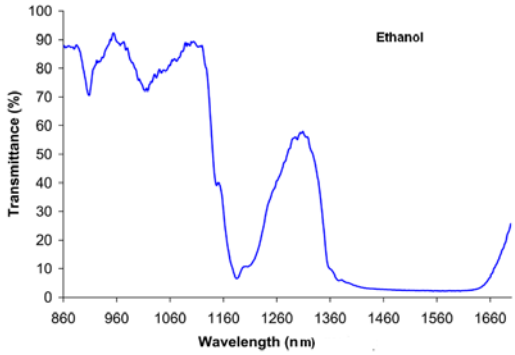

Fig. 5. The transmission spectrum of Ethanol in NIR

The ultra-pure water also absorbs at 970 nm and 1.18 μm, as it is shown the Fig. 6.

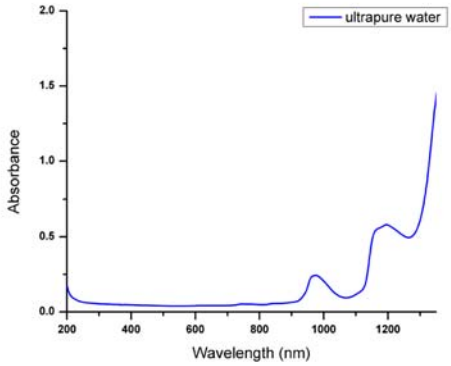

Fig. 6. The absorption spectrum of ultrapure water

We exposed Aetoxisclerol 2% commercially available at the laser beam emitted by a pulsed Nd:YAG laser at 1.06μm, between 2 min and 30 min. Following the irradiation, the absorption spectra of the medicine was measured (Fig. 7).

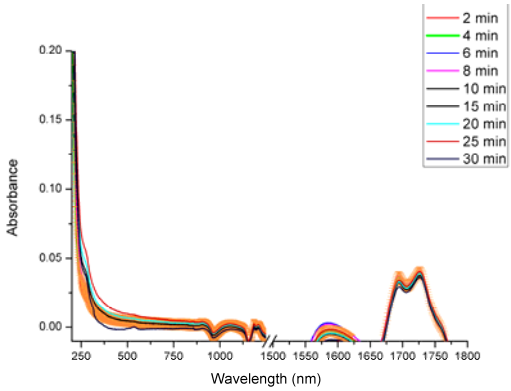

Fig. 7. The absorption spectra of Aetoxisclerol 2% exposed to 1.06 μm Nd:YAG laser radiation

These spectra indicate that for wavelengths that exceed 500 nm they remain within the measuring errors limits. We assume that in the spectral range (1000-1100) nm the absorption is due rather to the main chromophores in the tissue (melanine, water and hemoglobin/ oxihemoglobin; methemoglobin, in particular, has an overall absorption three times higher than oxihemoglobine in this spectral range) than Polidocanol proper.

Derivatives of blood hemoglobin, molecular oxygen dissolved in all components of the biological tissue, different ferments and other tissue substances that absorb light are considered as primary photoacceptors. Several photoinduced processes are known to take place during irradiation of an organism, such as photodissociation of oxyhemoglobin and the light-oxygen effect [15]. Both mechanisms involve the absorption of light and the formation of oxygen in different forms which have a biological effect. The efficiency of these processes depends quantitatively on the way light propagates in the tissues and the resultant absorption coefficients of individual chromophores in the cutaneous covering and in the tissue as a whole.

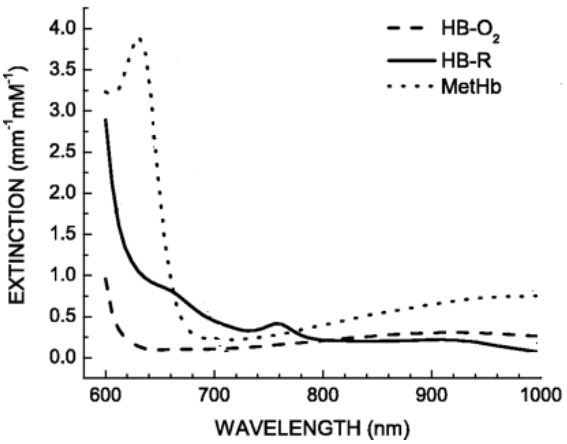

Fig. 8. The absorption spectra of Hemoglobin (HB-R), Oxihemoglobin (HB-O_2) and Methemoglobin (MetHb)

Modifications above the error limits are obtained in the spectral range (250-270) nm, as it is shown in detail in Fig. 7 and they may be due to the changes in the molecular structure of Polidocanol. A possible explanation is that nonlinear absorption effects take places in the tissue such as absorption of 4 photons at 1.06 μm, which would correspond to a transition at 265nm and which may be responsible for further effects on the tissue. The mechanisms of interaction of the laser radiation with the investigated solution are not completely elucidated and it is expected that further studies give a better understanding of them.

5. Conclusions

Comparing the spectroscopic measurements data with the clinical experimental results obtained at Instituto Médico Vilafortuny, we might conclude that the improvement of the action of Polidocanol, commercially available as Aetoxisclerol 2% on the varicose vein by exposure of the impregnated tissues to 1.06μm laser beam is possible due to the following mechanisms:

- at λ around 250nm, the laser radiation may be absorped by the Polidocanol proper. The mechanisms of interaction between the veins tissues and the medicine under the influence of laser radiation are not elucidated yet, but it is possible that nonlinear absorption effects take places in the tissue such as absorption of 4 photons at 1.06 μm (which would correspond to a transition at 265nm), which may be responsible for further effects on the tissue;

- at λ=1.06μm the absorption may be produced by the Ethyl alcohol and the main chromophores such as Hemoglobin, especially Methemoglobin and Melanin [16-18]; this may contribute to the sclerosis of the veins in the exposed area but it remains to clarify the possible mechanisms which lead to this effect.

In practice, physicians who use laser irradiation of the organism for therapeutic purposes often proceed empirically, relying on their personal experience and statistically accumulated information. They do not have a physically well-founded quantitative instrument which would permit an analysis of the significance of these processes as a function of the spectral range of the irradiating light, its duration, or power. In addition, the development of a physical basis for the interaction of light with such an object as the biological tissue and the development of recommendations for the optimal interaction parameters are of fundamental scientific interest for medical applications.

Acknowledgements

This research work was supported by the ANCS (RO), projects LAPLAS 3-PN 09 33, PALIRT 41-018/2007 and COST P21-Physics of Droplets

References

[1] D. J. Tibbs, Varicose Veins, venous disorders and lymphatic problems in the lower limb, 13:23 Oxford University Press (1997).

[2] T. Nijsten, Renate R. van den Bos, M. P. Goldman, M. A. Kockaert, T. M. Proebstle, E. Rabe, N. S. Sadick, R. A. Weiss, M. H. A. Neumann, J. Am. Acad. Dermatol. **60**, 1 (2009).

[3] K. Parsi, T. Exner, D. E. Connor, D. D. F. Ma1, J. E. Joseph, Eur. J. Vasc. Endovasc. Surg. **34**, 731 (2007).

[4] J. Alos, P. Carren, J.A. Lopez, B. Estadella, M. Serra-Prat, J. Marinello, Eur. J. Vasc. Endovasc. Surg. **31**, 101 (2006).

[5] J. H. Kunishige, L. H. Goldberg, P. M. Friedman, Clinics in Dermatology **25**, 454 (2007).

[6] Divya Railan, E. C. Parlette, N. S. Uebelhoer, T. E. Rohrer, Laser treatment of vascular lesions, Clinics in Dermatology **24**, 8 (2006).

[7] M. A. Trelles, I. Allones, X. Alvarez, M. Vélez, C. Buill, R. Luna, O. Trelles, Medical Laser Application **20**, 255 (2005).

[8] P. Redondo, J. Cabrera, Microfoam Sclerotherapy, Seminars in Cutaneous Medicine and Surgery (2005);

[9] P. Santos, A. C. Watkinson, J. Hadgraft, M. E. Lane, Skin Pharmacol. Physiol. **21**, 246 (2008).

[10] P. Ouvry, F.-A. Allaert, P. Desnos, C. Hamel-Desnos, Eur. J. Vasc. Endovasc. Surg. **36**, 366 (2008).

[11] K. Hartmann, L. Harms, M. Simon, Eur J Vasc Endovasc Surg **38**, 648 (2009).

[12] T. Yamaki, M. Nozaki, H. Sakurai, M. Takeuchi, K. Soejima, T. Kono, Eur. J. Vasc. Endovasc. Surg. **37**, 343 (2009).

[13] C. Hamel-Desnos, P. Ouvry, J.-P. Benigni, G. Boitelle, M. Schadeck, P. Desnos, F.-A. Allaert, Eur. J. Vasc. Endovasc. Surg. **34**, 723 (2007).

[14] Aethoxysklerol - Substance Summary, http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=7849055&loc=es_rss

[15] V. V. Barun, A. P. Ivanov, Journal of Applied Spectroscopy **77**, 1, (2010).

[16] W. G. Zijlstra, A. Buursma, W. P. Meenwsen-van der Roest, Clin. Chem., **37**(9), 1633 (1991).

[17] L. L. Randeberg, J. H. Bonesrønning,, M. Dalaker, J. S. Nelson, L. O. Svaasand, Lasers in Surgery and Medicine **34,** 414 (2004).

[18] J. Lee, N. El-Abaddi, A. Duke, A. E. Cerussi, M. Brenner, B. J. Tromberg, J Appl Physiol **100,** 615 (2006).

*Corresponding author: adriana.smarandache@inflpr.ro