Nanomedicine in oral cancer: photodynamic activity using chloroaluminum phthalocyanine-loaded PLGA-nanocapsules

Leonardo B. Paula[1] (PQ), Maryanne T. de Melo[1] (PG), Leonardo P. Franchi[1] (PQ), Antonio C. Tedesco[1*] (PQ)

[1]*Universidade de São Paulo, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Departamento de Química, Centro de Nanotecnologia e Engenharia Tecidual*

atedesco@usp.br

Keywords: *Oral cancer, Drug delivery system, Photosensitizer.*

Abstract

We report the studies using metastatic oral squamous cell carcinoma and fibroblast cell lines treated by chloroaluminum phthalocyanine, a photoactive drug loaded in nanocapsules of poly(lactic-coglycolic acid).

Introduction

Cancers of the oral cavity are the sixth most common cancers in the world. Unfortunately the number of cases continues to grow very fast with moderate survival rates, despite the recent advances in surgery and radiotherapy [1]. Also, it is well documented that increased tumour size is related to local and regional disease spread, higher recurrence rates and poor prognosis [1,2]. Photodynamic therapy (PDT) is a proposed trial protocol that uses cytotoxic free radicals produced by light activation of a sensitive drug known as a photosensitizer. The light used was in an appropriate wavelength. The poly(lactic-coglycolic acid) (PLGA) nanocapsules (NC) loaded with the PS was obtained by a type of oil in water (o/w) emulsion with a high thermodynamic stability. The development of nano-drug delivery (DDS), which are able to deliver cytotoxic molecules selectively to the target tissue while controlling the kinetics aspects, is currently one of the most active areas of cancer research.

Results and Discussion

In vitro studies were carried out the oral squamous cell carcinoma (OSCC) as a biological model. The cytotoxicity index of the NC, at fixed chloroaluminum phthalocyanine (ClAlPc) concentration, was first evaluated. The results showed a total biocompatibility at 0.5 µmol/L NC/ClAlPc, resulting in a cellular viability higher than 90% as expected. The cellular viability was obtained by MTT assay. Evaluation of the PDT light effects was performed using a typical clinical diode-laser operating at 500 mW @ 660 nm output power at a doses range from 100, 200 and 700 mJ/cm^2. The cellular viability decreased as a function of the irradiation dose. Mitochondrial activity describes a cellular viability of 62% compared to the absence of light activation of the PS (OSCC cells on DMEM 3%), which is related to the association of the effects of photodamage based on photodynamic mechanisms and cell injury. These results demonstrate that the formulation is promising as a DDS useful for oncology based in the PDT trials clinical. Our findings support the conclusion of the efficacy of phototherapy in the inactivation of most malignant cells in the cultured cell linage.

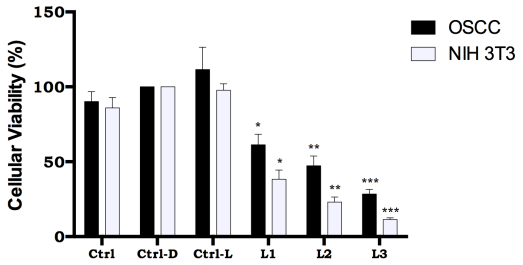

Figura 1. Cellular viability *in vitro* irradiation dosages in OSCC and NIH3T3 at 24h stage by MTT assay. Ctrl: control cells; Ctrl – D: cells incubated with NC/ClAlPc in the absence of photodynamic therapy (darkness); Ctrl – L: cells in the presence of only photodynamic therapy (light: 700 mJ/cm^2) and variation of irradiation dosages (L1: 100mJ/cm^2; L2: 200mJ/cm^2 and L3: 700mJ/cm^2). Statistical analysis was performed by one-way analysis of variance (ANOVA) and Tukey test. All data were expressed as the mean ± SEM of three independent experiments, *;**;***p<0.05.

Conclusion

Photodynamic therapy is an appropriate stand-alone intervention, or as an adjunct protocol to surgery. It is minimally invasive and can be applied repeatedly at the same site with no cumulative toxicity. This modality causes tissue destruction via the interaction between oxygen (in tumour tissue), light (at specific wavelength) and release of photosensitizing drug nanoentrapped.

Acknowledgements

We thank the Brazilian agencies for financial support. L.B.P., L.P.F. and A.C.T. were funded by the FAPESP Post-Docs projects 15/18684-9 and 14/11870-9 and thematic project 13/50181-1.

[1] Jerjes, W.; Hamdoon, Z.; Hopper, C. *Head Neck Oncol.* **2012**, *4(1)*, 3284.

[2] Specenier, P. M.; Vermorken, J. B. *J. B. Oral Oncol.* **2009**, *45*, 415.