Biodegradable ureteral stents for the treatment of urothelial tumors of the upper urinary tract cancer

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INTRODUCTION: Biodegradable ureteral stents have proven to be a useful alternative to conventional stents. Furthermore, they can be functionalized as drug eluting stents, especially for urothelial tumors of the upper urinary tract. In these cases, the conventional method of drug administration is via drug instillation. This has several drawbacks, such as high concentration dosage, increased side effects, short residence time and low bioavailability [1]. To avoid these problems, biodegradable ureteral stents impregnated by supercritical fluid CO_2 (SCF) with four different anti-cancer drugs were produced.

METHODS: Biodegradable ureteral stents were produced according previous work [2]**.** Four types of drug-eluting biodegradable stents based on natural polymers were prepared. The stents were impregnated by SCF (40°C, 100 bar, 90 min), with paclitaxel, epirubicin, doxorubicin and gemcitabine. The release kinetics of the impregnated drugs from the anti-cancer drug-eluting stents was evaluated in artificial urine solution (AUS) for 9 days. The anti-tumoral effect of the developed stents in transitional cell carcinoma (T24) and HUVEC primary cells, used as control, was evaluated.

RESULTS: The *in vitro* release study in AUS showed a sustainable release in the first 72h for the four drugs impregnated, after this time a plateau was achieved and finally the stent degraded after 9 days. To determine the sensitivities to each drug (IC50), a T24 cancer cell line was exposed to graded concentrations (0.01 to 2000 ng/ml) of the four drugs for both 4h and 72h. Additionally, toxicity as a result of both direct and indirect contact of the cell lines with the different material conditions of biodegradable stent were studied. The four anti-cancer drugs studied showed a concentration-dependent inhibitory effect on the T24 and (control) HUVEC cell lines with IC50's for paclitaxel of 7.30 ng and 501.50 ng, respectively. The T24 cancer cell line was shown to be more sensitive than the control HUVEC cell line for all the anti-cancer drugs tested.

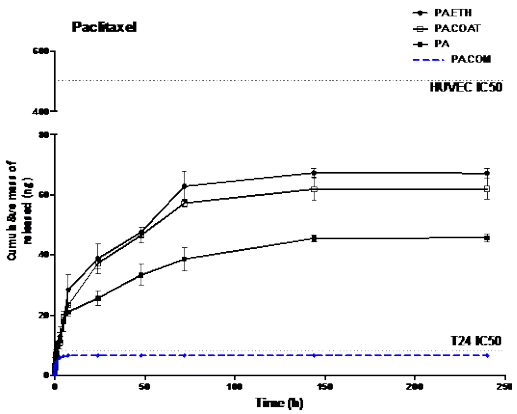

Fig. 1: *Release profile of the different stents impregnated with paclitaxel. Comparison with IC50 concentration for T24 and HUVEC cells.*

DISCUSSION & CONCLUSIONS: The direct and indirect contact of the anti-cancer biodegradable stents with the T24 and HUVEC cells confirm the anti-cancer effect of the stents impregnated with the four anti-cancer drugs, reducing approximately 75% of the viability of the T24 cell line after 72h and no negative effect in the HUVEC cells for the total drug release from stents. This study has thus shown the efficacy of the anti-cancer drug eluting biodegradable stents *in vitro* for the T24 cell line, with no toxicity observed in non-cancerous HUVEC cells.

REFERENCES:[1]Audenet F (2013) World J. Urol. [2]Barros AA, (2015) Int. J. Pharm

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