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Novel drug-eluting beads (DEBs) containing tyrosine kinase inhibitors (TKIs) for cancer therapy

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DEBs are embolic agents that can be loaded with anti-cancer drugs which are subsequently released over time at the tumor site following administration into the arteries that feed liver malignancies using a technique known as transarterial chemoembolization (TACE). The most commonly loaded drugs into DEB are doxorubicin and irinotecan, both cytotoxic agents that interfere with DNA replication. However, it is also possible to load DEB with certain targeted agents such as TKIs. Due to the chemical structure and properties of these compounds, it is necessary to use different methodological approaches to incorporate them into the bead matrix. We describe the loading of DC Bead™ with vandetanib, an anti-angiogenic multi-targeted TKI. The molecule may exist in several pH-dependent charge states which affect both its solubility in water and capacity to occupy drug binding sites within the beads. Maximum drug loading capacity of vandetanib into DC Bead™ and a novel radiopaque version was investigated at varying pH. Uniform distribution of the drug throughout the bead was confirmed by SEM-EDX analysis. The effect of drug loading on physicochemical properties of the beads such as size, radiopacity and compressibility was examined as well as the characteristics of *in vitro* drug release. In order to mimic ischemia after embolization, the effect of vandetanib on HepG2 cell viability under hypoxic conditions was investigated by MTT assay. Vandetanib showed equipotency in hypoxia and normoxia across a range of concentrations with an IC₅₀ of approximately 6.25 μM, confirming its suitability for delivery from a DEB.

Biography

Alice Hagan is a Scientist at Biocompatibles UK Ltd and currently pursuing PhD at the University of Brighton. Her research focuses on novel drug-device combinations for the treatment of liver tumors. In 2014, she was awarded an Industrial Fellowship from the Royal Commission for the Exhibition of 1851, in order to pursue her research and development of drug-eluting bead products in partnership with Biocompatibles.

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