Kinetic targeting of intravascular triggered drug delivery system

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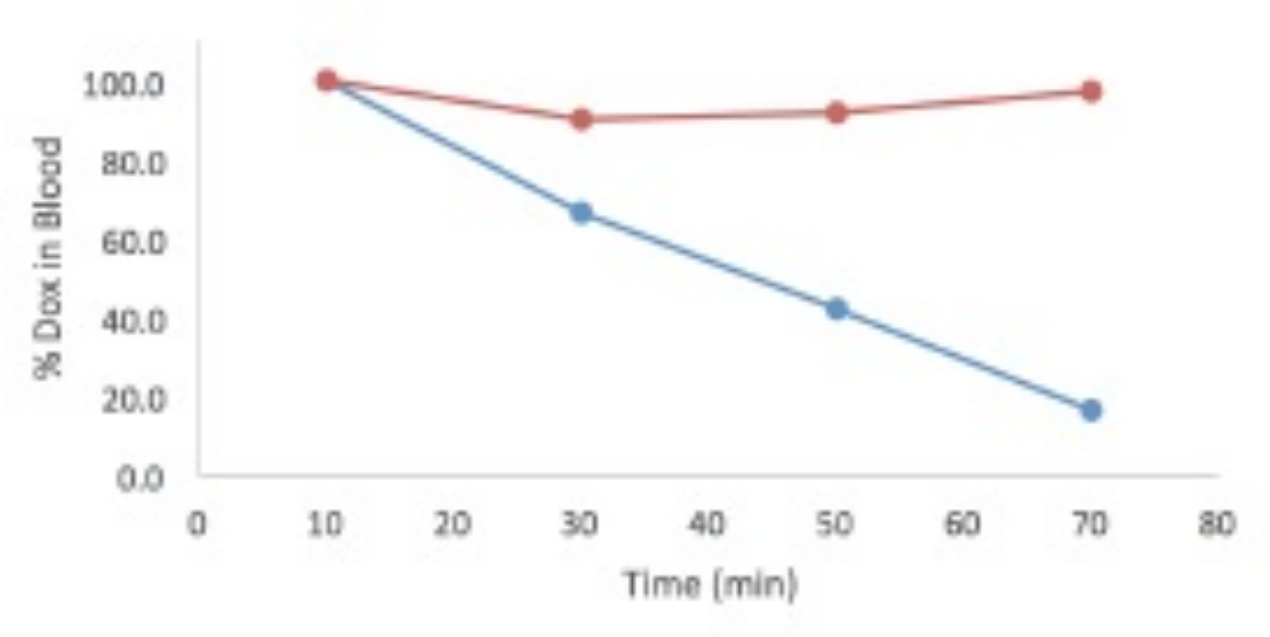
Technology description

Device for Vascular Filtration of Excess Chemotherapeutic Containing Thermally Sensitive Liposomes via Kinetic Targeting

Technology:
Researchers at MUSC have created a device and method that can remove excess chemotherapeutic containing Intravascular Triggered Drug Delivery Systems (IVDDSs) that are utilized in localized drug treatment, thus greatly reducing treatment toxicity and side effects without diminishing the effectiveness.
The filtration device connects directly to an artery in order to provide a consistent blood supply to the device. The blood is pumped through a heat exchanger that heats the blood to 41-42 ºC to release the therapeutic contained in the IVDDS, in this case a thermally sensitive liposome (TSL). The blood is then pumped through a filter that is specific for the therapeutic contained in the TSLs and the excess therapeutic is removed. Lastly, the blood is cooled to 37 ºC and returned to the body. In human patients, a single double-lumen catheter may be used to both access and return blood.
The filtration device is connected to the patient after the completed delivery and activation of the IVDDS, in this case TSLs. Once the trigger is removed that precipitated the activation and localized release of the drug to the desired location the treatment is complete, however excess TSLs containing therapeutic payload remain in the circulatory system. To prevent the degredation of these excess TSLs and the subsequent toxicity from the therapuetic payload, the filtration device removes these TSLs from the blood stream. A test with a prototype device in animal models demonstrated that the filtration device can remove the excess TSLs almost completely within 60 minutes resulting in drastically lower levels of the therapeutic in the blood stream following treatment (blue) as compared to treatment without subsequent filtration (red). This filtration device provides the opportunity to signficantly reduce the toxicity of IVDDS treatment without hindering the effectiveness. The device may also enable administration of a higher dose than currently used, since part of the administered dose is again removed. Administration of a higher dose will result in delivery of larger drug amount to the targeted tissue (e.g. tumor).



Overview:

IVDDSs are utilized for a variety of treatments to provide localized therapeutic delivery, with one of the most common applications being the localized treatment of cancerous tumors. IVDDS are administered systemically (e.g. intravenous infusion) and circulate within the systemic blood circulation. Depending on the type of IVDDS, release of the drug is triggered within the target region by the appropriate trigger signal (e.g. via localized heating for temperature sensitive liposomes (TSL), or ultrasound for microbubble based IVDDS). Dependent on IVDDS, the trigger signal can be applied externally or internally (heat, ultrasound, light, etc.), or can be a biological signal specific to the targeted tissue (e.g. pH). Following the localized drug release within the vasculature, drug is extracted by targeted tissue and taken up by cells within the target region. Unique to IVDDS, drug uptake by cells is limited to the duration when the trigger for release is applied, e.g. 30-60 minutes in prior studies. For comparison, other DDS such as conventional liposomes typically require many hours or days to accumulate in the target region, and release the drug at similar slow rate.

Toxicity results from uptake of DDS and/or drug in non-targeted tissue regions. The proposed method removes any drug still present in systemic circulation from the body after triggered release and uptake by cells in the target region has occurred, thus avoiding any toxicity from IVDDS that did not completely release their content (which includes the majority of administered drug), without affecting efficacy. Since with the proposed approach IVDDS are present within the systemic circulation only for a limited duration (-hours), toxicity is greatly reduced.

Application area

Localized drug treatments, IVDDS, cancer treatment

Advantages

Reduced toxicity:By removing excess IVDDS after the completion of treatment, the filtration system greatly reduces the systemic toxicity following treatment.
Increased Payload:Since part of the administered drug is again removed, this may also allow administration of higher doses than currently used.
No reduction in efficacy:As the filtration device is utilized after the treatment is complete there is no reduction in treatment efficacy.
Ease of Use:The device only requires connection to a single artery to supply the blood and a single vein to return the blood.

Institution

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