# Targeted delivery of doxorubicin through conjugation with cathepsin B-cleavable peptide

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## Abstract

Cancer nanomedicine using nanoparticle-based delivery systems has shown remarkable promise in recent decades for improving anticancer treatment. However, limited targeting efficiency, low drug loading efficiency and innate toxicity of nanoparticles have caused severe problems, leaving only a few available in the clinic. Here, we newly developed carrier-free nanoparticles of cathepsin B-cleavable peptide (Phe-Arg-Arg-Gly; FRRG)-conjugated doxorubicin (DOX) prodrug (FRRG-DOX) that formed a stable nanoparticle structure with an average diameter of 213 nm in aqueous condition. The carrier-free nanoparticles of FRRG-DOX induced cytotoxicity against cathepsin B-overexpressed tumor cells whereas the toxicity was minimized in normal cells. In particular, the FRRG-DOX nanoparticles showed the successful tumor-targeting ability and enhanced therapeutic efficiency in human colon adenocarcinoma (HT-29) tumor-bearing mice via enhanced permeation and retention (EPR) effect. Furthermore, FRRG-DOX nanoparticles did not present any severe toxicity, such as non-specific cell death and cardiac toxicity, in normal tissues due to minimal expression of cathepsin B. Our new carrier-free FRRG-DOX nanoparticles could solve many serious problems of current cancer nanomedicine, including non-specific targeting in normal tissues, low drug loading efficiency, native toxicity of nanoparticles, and difficulty in mass production and for clinical applications.

***Keywords:*** *nanoparticle, doxorubicin, carrier-free, selective toxicity*

## References

[ 1 ] Shim, M. K., Park, J., Yoon, H. Y., Lee, S., Um, W., Kim, J., . . . Kim, K. (2019). Carrier-free nanoparticles of cathepsin B-cleavable peptide-conjugated doxorubicin prodrug for cancer targeting therapy. Journal of Controlled Release, 294, 376-389.

## Biography

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