Peripheral nerve injury has seriously affected people's health and life. Nerve growth factor (NGF) is essential for neurons to promote their development, differentiation, growth, regeneration and other functional properties. NGF is found to induce the growth of nerve fibers directionally [1, 2]. In the previous study, the graphene oxide/polyacrylamide (GO/PAM) composite hydrogels were successfully prepared, and it was found that the composite hydrogel with 0.4% GO (GO.4) could effectively promote the growth and proliferation of Schwann cells. However, the effect is weakened after long periods of culture [3]. Thus, in the present study, the GO/PAM composite hydrogel incorporated with nerve growth factor was further fabricated to study its effect on Schwann cells for long time culture. The contact angle measurements were employed to test whether the addition of NGF could promote hydrophilic properties of the original GO/PAM hydrogels. The mechanical property and the degradation behavior were also characterized. The release of NGF from GO/PAM hydrogels was measured. Furthermore, the composite hydrogel was co-cultured with Schwann cells to evaluate the effects of the composite hydrogel incorporated with NGF on the attachment and proliferation of Schwann cells thoroughly. The results showed that with the increasing contents of NGF, the surface of the composite hydrogel had no obvious changes. The hydrophobicity and mechanical properties of hydrogel also had a little difference. The release of NGF could be well and easily controlled by varying the fabrication parameters of the composite hydrogel. Besides, the co-culture of Schwann cells showed that the more incorporated NGF, the better growth they promoted. This study may provide an important theoretical basis for the design and development of tissue engineering scaffolds, and an understanding of nerve growth factor's application, which may have potential application for peripheral nerve regeneration.

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References

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Rapamycin loaded magnetic graphene oxide nanoparticles as tumor-targeted drug delivery system: synthesis and in vitro characterization

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With the development of nanotechnology, many kinds of functional targeted nanoparticles have been applied for cancer treatment. Among these different nanoparticles, graphene oxide modified with iron oxide nanoparticles (Fe3O4/GO) have attracted much attention for applications in targeted drug delivery because they could carry drug molecules through π-π interactions, electrostatic attraction or chemical bond and could be magnetically guided to the targeted organs or lesion sites inside the body [1, 2]. Herein, the Fe3O4/GO nanoparticles were firstly prepared by hydrothermal method using FeSO4·7H2O as the iron source and H2O2 as the oxidant. Then, a tumor-targeted drug delivery system was designed using Fe3O4/GO as a platform and rapamycin (Rapa) as an anticancer drug (Fig. 1a). The results showed that the drug loading content and entrapment efficiency were 23.93 ± 3.72%, 91.68 ± 3.31%, respectively. The in vitro drug release profiles of Fe3O4/GO-Rapa nanocomposites exhibited a biphasic pattern with an initial fast release phase followed by a slower release phase at pH 7.4 (Fig. 1b). The Fe3O4/GO-Rapa could inhibit the proliferation and induce greater
apoptosis of HepG2 cells in comparison with free Rapa, which displayed time or concentration-dependent (Fig. 1c). Overall the preliminary studies showed that Fe3O4/GO-Rapa nanocomposites can be a potential candidate for magnetic-targeting tumor-specific drug delivery in the tumor diagnostic and therapy.

**Keywords**: magnetic graphene oxide nanocomposites, Rapamycin, in vitro drug release, cell vitality

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**References**


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An intelligent doxorubicin prodrug with GRP78 recognition and sequential targeting ability to tumor cell membrane and nucleus

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Nanoscale drug delivery systems could endow the antitumor agents with passive and active targeting ability [1]. However, these nanomedicines developed to date mainly transport drugs to the cytoplasm rather than the nuclei, but the sites of action of many first-line anticancer drugs such as doxorubicin (DOX) and camptothecin (CPT) are localized in nucleus. GRP78 (glucose regulated protein of 78 kDa) is a member of the heat shock protein 70 (HSP70) family that mainly locates in endoplasmic reticulum (ER) and involves in protein folding and assembly. Recent evidence indicates that the overexpressed GRP78 can be translocated to cell surface. And the finding that cell-surface GRP78 is preferentially present in cancer cells makes it a potential target for cancer therapy [2]. Herein, an intelligent DOX prodrug (IDP) was synthesized by conjugating DOX and a bifunctional peptide (WIFPWIQLKKKRKVC) to the two end of heterofunctional poly(ethylene glycol) (Maleimide-PEG-COOH) (Fig. 1). The bifunctional peptide is composed of a GRP78 binding sequence WIFPWIQL and a nuclear localization signal sequence KKKRKVC. The IDP could efficiently and sequentially enter the tumor cell membrane and nucleus under the guidance of the bifunctional peptide as observed by confocal laser scanning microscope. In vitro antitumor study revealed that IDP exhibited an enhanced cytotoxicity against colorectal cancer cells (high level of cell surface GRP78). Further studies will be conducted to evaluate the in vivo antitumor efficiency of IDP. Together, these results demonstrate that the DOX prodrug developed in this study holds great promise to be used as an effective anticancer agent with negligible side effects.

**Keywords**: GRP78, doxorubicin, prodrug, sequential targeting

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**References**


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Janus-faced and pH-responsive nanohybrids for synergistic targeted drug delivery

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Nanoscale drug delivery systems could endow the antitumor agents with passive and active targeting ability [1]. However, these nanomedicines developed to date mainly transport drugs to the cytoplasm rather than the nuclei, but the sites of action of many first-line anticancer drugs such as doxorubicin (DOX) and camptothecin (CPT) are localized in nucleus. GRP78 (glucose regulated protein of 78 kDa) is a member of the heat shock protein 70 (HSP70) family that mainly locates in endoplasmic reticulum (ER) and involves in protein folding and assembly. Recent evidence indicates that the overexpressed GRP78 can be translocated to cell surface. And the finding that cell-surface GRP78 is preferentially present in cancer cells makes it a potential target for cancer therapy [2]. Herein, an intelligent DOX prodrug (IDP) was synthesized by conjugating DOX and a bifunctional peptide (WIFPWIQLKKKRKVC) to the two end of heterofunctional poly(ethylene glycol) (Maleimide-PEG-COOH) (Fig. 1). The bifunctional peptide is composed of a GRP78 binding sequence WIFPWIQL and a nuclear localization signal sequence KKKRKVC. The IDP could efficiently and sequentially enter the tumor cell membrane and nucleus under the guidance of the bifunctional peptide as observed by confocal laser scanning microscope. In vitro antitumor study revealed that IDP exhibited an enhanced cytotoxicity against colorectal cancer cells (high level of cell surface GRP78). Further studies will be conducted to evaluate the in vivo antitumor efficiency of IDP. Together, these results demonstrate that the DOX prodrug developed in this study holds great promise to be used as an effective anticancer agent with negligible side effects.

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