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Hyaluronic Nanogels and Flavonoid-Assisted Chemotherapy as a Combined Anti-Melanoma Approach

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Introduction

Melanoma, a highly aggressive form of skin cancer, poses significant challenges due to its metastatic potential and resistance to conventional treatments, contributing to approximately 75% of skin cancer-related deaths globally. Traditional therapies, including surgery, chemotherapy and immunotherapy, often face limitations such as systemic toxicity, poor drug bioavailability and Multi Drug Resistance (MDR). Recent advancements in nanomedicine, particularly Hyaluronic Acid (HA)-based nanogels, combined with flavonoid-assisted chemotherapy, offer a promising approach to overcome these hurdles. HA nanogels leverage the overexpression of CD44 receptors on melanoma cells for targeted drug delivery, while flavonoids, natural compounds with antioxidant and anti-cancer properties, enhance chemotherapeutic efficacy. This essay explores the synergistic potential of HA nanogels and flavonoids in improving melanoma treatment outcomes through precise drug delivery and resistance modulation [1].

Description

Hyaluronic acid nanogels are biocompatible, pH-responsive and enzymatically degradable carriers designed to deliver chemotherapeutic agents directly to melanoma cells. These nanogels exploit the CD44 receptor, overexpressed in melanoma, for targeted uptake, ensuring high drug accumulation at tumor sites. For instance, studies have demonstrated that HA-based nanogels loaded with Doxorubicin (DOX) exhibit pH-sensitive release, triggered by the acidic tumor microenvironment, resulting in enhanced intracellular drug concentrations and reduced systemic toxicity. Research by Chen et al. showed that HA nanogels conjugated with cationic bovine serum albumin and paclitaxel achieved a lower IC50 value (12.96 µg/ml) compared to non-targeted variants, highlighting their efficacy in CD44-targeted therapy. Additionally, HA nanogels can incorporate stimuli-responsive features, such as Near-Inf Rared (NIR)-induced hyperthermia, to reverse MDR by suspending drug efflux, as seen in studies with gold nanorods-loaded HA nanogels. These properties make HA nanogels ideal for delivering chemotherapeutic drugs like 5-Fluoro Uracil (5-FU) or DOX with improved specificity and reduced side effects.

Flavonoids, such as quercetin and curcumin, enhance chemotherapy by modulating resistance mechanisms and amplifying anti-cancer effects. These natural compounds inhibit drug efflux pumps, reduce oxidative stress and induce apoptosis in melanoma cells. For example, a study combining curcumin with HA nanogels for photothermal therapy demonstrated significant tumor growth inhibition in melanoma-bearing mice. Flavonoids also synergize with chemotherapeutic agents by sensitizing cancer cells to drugs, thereby lowering the required dose and minimizing toxicity. Recent research highlights the use of HA nanogels co-loaded with DOX and flavonoids, achieving sustained release and enhanced cytotoxicity in vitro against melanoma cell lines like A375. The integration of flavonoids with HA nanogels not only improves drug bioavailability but also leverages their anti-inflammatory and antioxidant properties to mitigate chemotherapy-induced damage to healthy tissues, offering a dual therapeutic advantage [2].

Conclusion

In summary, the combination of hyaluronic acid nanogels and flavonoid-assisted chemotherapy represents a transformative approach to melanoma treatment. HA nanogels provide targeted, stimuli-responsive drug delivery, addressing challenges like poor bioavailability and MDR, while flavonoids enhance chemotherapeutic efficacy through resistance modulation and synergistic anti-cancer effects. This integrated strategy improves tumor-specific drug accumulation, reduces systemic toxicity and holds promise for clinical translation. By harnessing the unique properties of HA nanogels and flavonoids, this approach paves the way for more effective, safer and patient-compliant melanoma therapies.

Acknowledgement

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Conflict of Interest

None.

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