

## Review Form 1.7

Journal Name:	<b>Journal of Pharmaceutical Research International</b>
Manuscript Number:	<b>Ms_JPRI_102290</b>
Title of the Manuscript:	<b>Surface-Decorated Nanocarrier as a Targeted Drug Delivery Cargo to Folate Receptor-Overexpressing Cells for Auspicious Anti-cancer and Anti-inflammatory Activity</b>
Type of the Article	<b>Original Research Article</b>

### **General guideline for Peer Review process:**

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<https://www.journaljpri.com/index.php/JPRI/editorial-policy> )

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### PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<p><b>Compulsory</b> REVISION comments</p> <ol style="list-style-type: none"> <li>1. <b>Is the manuscript important for scientific community?</b> (Please write few sentences on this manuscript)</li> <li>2. <b>Is the title of the article suitable?</b> (If not please suggest an alternative title)</li> <li>3. <b>Is the abstract of the article comprehensive?</b></li> <li>4. <b>Are subsections and structure of the manuscript appropriate?</b></li> <li>5. <b>Do you think the manuscript is scientifically correct?</b></li> <li>6. <b>Are the references sufficient and recent? If you have suggestion of additional references, please mention in the review form.</b></li> </ol> <p><b><u>(Apart from above mentioned 6 points, reviewers are free to provide additional suggestions/comments)</u></b></p>	<ol style="list-style-type: none"> <li>1. This manuscript describes a study that aims to develop a targeted nanocarrier loaded with methotrexate (MTX) to improve its therapeutic efficacy and minimize toxicity. The nanocarrier is designed to specifically target cells that overexpress the folate receptor (FR), such as cancer cells and activated macrophages involved in rheumatoid arthritis (RA). The authors synthesized and characterized a folic acid-chitosan (FA-CS) conjugate and used it to coat MTX-loaded nanoparticles (NPs) made of poly(D,L-lactide-co-glycolide) (PLGA). The formulation with the best performance, referred to as F10, was selected for further evaluation through in vitro and in vivo studies. The results demonstrate that F10 had satisfactory encapsulation efficiency, a homogenous particle size, and a positive zeta potential. The nanocarrier exhibited a biphasic drug release pattern in different pH conditions, confirming successful MTX incorporation into the polymeric matrix. In vitro cytotoxicity assays showed that F10 displayed an improved anticancer effect on FR-positive cancer cells compared to free MTX or uncoated MTX NPs. However, no significant effect was observed in FR-negative cells. The stability of F10 was also assessed, showing good storage stability at refrigerated temperature for up to 3 months. Furthermore, in an animal model of complete Freund's adjuvant (CFA)-induced RA in mice, oral administration of F10 demonstrated significant therapeutic benefits and reduced systemic toxicity compared to conventional pure MTX or commercial MTX tablets. Overall, the study presents a promising approach in developing a targeted nanocarrier for the delivery of MTX, enhancing its efficacy against FR-overexpressing cancer cells, and potentially offering a novel oral treatment option for RA and other inflammatory conditions associated with FR-overexpressing activated macrophages.</li> <li>2. Title of the manuscript looks good, except the <b>Auspicious</b> word.</li> <li>3. Abstract is comprehensive.</li> <li>4. Subsections and structure of the manuscript is appropriate</li> <li>5. Manuscript is scientifically correct</li> <li>6. Authors can add few more recently published work on FA-CS and nanocarriers. For example: doi.org/10.1021/acsbiomaterials.9b00112</li> <li>7. Additional comments:             <ol style="list-style-type: none"> <li>1. This study presents a well-executed and highly promising approach in the development of a targeted nanocarrier for drug delivery to FR-overexpressing cells. The research findings not only contribute to the advancement of nanomedicine but also hold great potential for improving anticancer and anti-inflammatory therapies, with implications for personalized medicine and precision treatment approaches</li> <li>2. Discuss the mechanism of enhanced cytotoxicity in FR-positive cells: Elaborate on the potential mechanisms responsible for the enhanced cytotoxicity of the FA-CS coated MTX NPs formulation in FR-positive cells.</li> <li>3. Provide additional context for the choice of cell lines</li> </ol> </li> </ol>	
<p><b>Minor</b> REVISION comments</p> <ol style="list-style-type: none"> <li>1. <b>Is language/English quality of the article suitable for scholarly communications?</b></li> </ol>	YES	
<p><b>Optional/General</b> comments</p>		

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**PART 2:**

	<b>Reviewer's comment</b>	<b>Author's comment</b> <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
<b>Are there ethical issues in this manuscript?</b>	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	

**Reviewer Details:**

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