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Journal Name:	**Journal of Pharmaceutical Research International**
Manuscript Number:	**Ms_JPRI_79294**
Title of the Manuscript:	**FORMULATION DEVELOPMENT AND EVALUATION OF ITRACONAZOLE LOADED INVASOMES HYDROGEL**
Type of the Article	

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.
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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)*
Compulsory REVISION comments	In the Abstract, the word "candidasis" need to be corrected to "candidiasis", "aques" to more commune "aqueous" In the Introduction part: The word "trasdermal" need to be corrected to "transdermal". The phrase "Subsequently developed ethosomes, new soft vesicular carriers mainly consisting of phospholipids, ethanol and water [5]." This phrase must be rewritten. Because the author developed invasomes based hydrogels I think it is very important here to give a definition of "invasomes" and provide references related to the preparation and properties of these materials in order to integrate these materials in the state of the art of this new type materials related to the conventional ones. It is very weakly emphasized (in a single sentence) the main objective of the paper, the novelty degree and the particularities of this researches compared to other. In the literature there are a lot of researches related to the preparation and properties of invasome hydrogels. What brings new, the material prepared in this research compared to those already existing in the literature? Also there are studies related to the skin delivery of itraconazole using different types of hydrogels. Please highlight the novelty degree of the present study related to the existing one. I suggest a few references in which the authors prepare about the same material and the same drug release: • Invasome: A Novel Nanocarrier for Transdermal Drug Delivery Nanomaterials 2020, 10, 341; • Preparation and evaluation of curcumin invasomes, International Journal of Drug Delivery 6(2):113-120 • Nangare, S., Dugam, S. Smart invasome synthesis, characterizations, pharmaceutical applications, and pharmacokinetic perspective: a review. Futur J Pharm Sci 6, 123 (2020) • Nanoemulsion based Hydrogels of Itraconazole for Transdermal Drug Delivery, Journal of Scientific & Industrial Research Vol. 74, February 2015, pp. 88-92 • Microemulsion-based Hydrogel Formulation of Itraconazole for Topical Deliverym, Journal of Pharmaceutical Investigation,Volume 40 Issue 5 / Pages.305-311 / 2010 / 2093-5552 In the Experimental part: pH measurements "The electrode was dipped into the vesicles as long as covered by the vesicles. Then pH of selected formulation was measured and readings shown on display were noted" What is the aggregation state of the as prepared materials in this stage? If the material is not liquid or at least colloidal, the pH measurement is not very relevant. The pH of the vesicles may be different from the pH of the medium in which the vesicles are dispersed Drug content "Accurately weighed amount of hydrogel formulation equivalent to 20mg of topical hydrogel"	

	How the amount of hydrogel was accurately measured? Was the sample initially dry? Extrudability study "Extrudability was based upon the quantity of the hydrogel extruded from collapsible tube on application of certain load. More the quantity of hydrogel extruded shows better extrudability.It was determine by applying the weight on hydrogel filled collapsible tube and recorded the weight on which hydrogel was extruded from tube." This phrase must be rewritten; its meaning is not clearly understood. Spreadability IS the described Spreadability test a specific test for determining the properties of this kind of materials or is it a method of its own? Release kinetics "There are several models to represent the drug dissolution profiles where ft is the function of t (time) related to the amount of drug dissolved from the pharmaceutical dosage system" Please specify what ft is, because the function which describes the drug dissolution profiles is not clear. Equation (1) "Qt = Qo + Kot (1)" need to be rewrite with an Equitation program, because the "t" value can be confused in term Kot. "The first order Eq. (2) describes the release from the system where release is concentration dependent e.g. pharmaceutical dosage forms containing water soluble drugs in porous matrices." It is not clear what this equation describes. Please explain. All the other equations must be rewritten, the same problem like Eq. 1, need to be rewrite with an Equitation program. Equation (3) (Higuchi) has a name; the first two equations are not named? Korsemeyer-Peppas equation is not numbered. The equation must be numbered (4). Stability studies What is "accelerated stability test?" "Analysis of the samples were characterized for vesicle size and drug content after a period of 0, 15, 30, 60 and 90 days." How the particle size was determined, what method was used? Please provide here particle size measurement and correlation between of the particle size and the composition of the hydrogel. In Results and Discussions: "Formulation OIGF4 was found to be good Table 2" It is not very correct to say that only one of the samples is good. I would suggest saying that this sample provided the best results in terms of drug content, viscosity, spreadability, extrudability, gel strength. I also consider it important to explain the as obtained values and especially why these values are the optimal ones. "Results of In-vitro drug release from optimized formulation (OIGF4) are given in table 3…" I consider that a phrase should be introduced such as: "Based on best results in terms of drug content, viscosity, spreadability, extrudability, gel strength for the formulation OIGF4, this sample was chosen for estimation of in-vitro drug release, and the results are presented in…." "The in vitro drug release data of the formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic	

	equation and Korsmeyer's -pappas models in order to determine the mechanism of drug release" The expression "to goodness of fit test "is not the most correct, I suggest correcting it. I consider that the names of Figures 1-4 are not clear enough; they must emphasize the four applied models. Please correct them in order to easily follow which of the applied models shows the best behavior for in-vitro drug release using the hydrogel type material. Many measurements related to the properties of the hydrogel type materials (drug content, viscosity, spreadability, extrudability, gel strength) have been presented, but it is no connection between the composition of the tested samples and the properties of the as prepared materials. Please enter explanatory discussions related to these issues. No physical measurements (such as particle size measurements, zeta potential, and transmission electron microscopy) were performed to emphasize the structural and morphological properties of the as prepared hydrogel. These measurements are especially useful to be able to make correlations between the values of drug content, viscosity, spreadability, extrudability, gel strength and the composition of the material. Please provide at least two measurements that emphasize the structure and morphology of the as prepared hydrogels. It is also necessary to explain some aspects regarding: Why does this composition (formulation OIGF4) present the best results, (in term of the composition)? Is the drug release model (first order model of drug release kinetics) for the presented hydrogel material similar with other materials presented in the literature? What is new about this study, related to the release properties of the proposed drug compared to other variants already presented in the literature? Are these results sufficiently well supported for the application of the material for in vitro studies? Because this type of material is used to a drug release on the skin, nowhere is mentioned the biocompatibility properties of this material. Please specify and provide measurements to demonstrate these properties. In Conclusion part: Conclusion section is poor and not concluding. What important results were obtained? What novelties have been obtained compared to other researches. The references are relatively old, older than 2010, they need to be supplemented with new references, regarding the preparation of hydrogel type materials with applicability in the release of medicines.	

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Minor REVISION comments	The conceptualization of the article is not clear. In the literature there are a lot of researches related to the preparation and properties of invasome hydrogels. Also there are studies related to the skin delivery of itraconazole using different types of hydrogels. the composition of the materials are very similar with other samples presented in the literature and is not presented de effect of each component. No psychical measurements are providing to demonstrate the structure and morphology of the as prepared materials. The properties of the as prepared material, in term of drug content, viscosity, spreadability, extrudability, gel strength, are not correlated with the composition of the materials. One sample was chosen to be “good” and just for this the in-vivo drug study has applied without explaining why this sample is “good”, based on the as obtained results. No biocompatibility measurements are providing in order to support the applicability of this material for itraconazole release on the skin.	
Optional/General comments		

PART 2:

	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)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

As per the guideline of editorial office we have followed VANCOUVER reference style for our paper.

Kindly see the following link:
http://sciencedomain.org/archives/20

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