**Reviewer A**

**Question: 1**

It is strongly recommended to check the previous PDF version of revised and uploaded manuscript revision. I suppose that the authors did not ignore on purpose all the comments that were directly highlighted and commented in the whole manuscript. The authors were supposed to correct and accept both comments in PDF format manuscript and to answer to the questions separately written. Please, check it once again and revise.

**Answer 1:** Apply

**Question: 2**

Abstract has not been contracted and containing a lot of mistakes: "percentage of practical yield" need to be replased by "yield", scanning electron microscopy is repeating twice, I suppose that "DRX spectra" is actually XRD?!

**Answer 2:** Apply

**Question: 3**

The authors have not accepted reviewer suggestion: "In the revising document, please try to use integer to present the efficiency of encapsulation, yield, drug loading, diameter size and drug release (for example 94, 60, 71 % or 31 μm, etc.) both in the text and in the tables." It is strongly reccomended to revise both the text in the manuscript and the Table II.

**Answer 3:** Apply

**Question: 4**

 Also, in the Introduction section, sentences "Examples of such as..." from line 50 to line 56 still has no point and sence and requires revision. It is not acceptable to write a sentence without a verb and just to count polymers.

**Answer 4:** Apply

**Question: 5**

The first sentence in the Introduction part should be revised. "The technique of microencapsulation by solvent evaporation is widely applied in pharmaceutical industries to obtain the controlled release of drug. » It could only obtain the formulations for controlled release of drug. Also, the sentence «In this process..." it is not clear which process is discussing, is that a solution-evaporation method¬¬? Please, try to find more scientific term for "doughnut". It is also recommended to the authors to use whole construction for gastrointestinal tract, not an abbreviation.

**Answer 5:** Apply

**Question: 6.**

Further, the idea of using polymer blend of non-degradable and degradable polymers as drug carrier has not been highlighted very well. Maybe it would help if the authors check the following reference: "K. Manokruang, E. Manias, Hollow microspheres and aqueous phase behavior of pH-responsive poly(methylmethacrylate-co-methacrylic acid) copolymers with a blocky comonomer distribution, Materials Letters 63 (2009) 1144–1147".

**Answer 6:** thanks for the reference it helped me to clarify the use of PMMA and the explanation is given in the introduction.

**Question: 7**

In the revised manuscript, Table I still does not contain required and necessary data such as molecular weight of polymer used as matrix (replace from PMMA characterization into the Table). It is not enough just to write a polymer/drug ratio in the Table I. In addition, Table I caption should be replaced in Experimental part (preparation of microspheres section).

**Answer 7:** Apply

**Question: 8**

The sentence "Whereas HCTZ loaded values increased when the microspheres were PCL-based or the two polymers combined (EC / PCL)." is not grammatically correct and requires revision. The authors need to better explain what the reason of such a behavior was: small drug loading with EC matrix and higher DL obtained with PCL/EC matrix. From the results presented in Table II, it seems that for PMMA based microspheres, with the increase of PMMA viscosimetric mass, drug loading increased and the yield decreased. The authors claimed that both DL and yield increase. Please, revise those conclusions.

**Answer 8:** Apply inresults and discussion

**Question: 9**

The authors have not answered to the question (question 11): "In the part of SEM analysis results, the authors explained the irregular shape of the obtained microspheres with PMMA as followed: "There are forms of sticks in the three batches which may correspond to the PMMA matrix not incorporated in the microspheres." How can be explained this (incompatibility between different polymers in blends)". This part was erased and reorganized, which is not a common procedure in revising a manuscript. Anyway, an answer to the question: «Why the authors did not prepare PMMA-HCTZ microspheres since the all other (EC, PCL, EC/PCL) were prepared." is not satisfactory and requires further explanation. In addition, the sentence: "However, the microparticles containing EC and β-CD (Fig.1-7) appear spherical, of porous surface and containing powders at the surface which can correspond to the drug." was erased too and in a new manuscript the remainance of the drug has not been mentioned at all. The authors just mentioned the revision of particles size.

**Answer 9**

About this part that's what I found as an answer regarding the incorporation of HCTZ into matrices containing PMMA and I found this explanation in reference [33]. If you can help me find another explanation for this phenomenon will be a plus for my article. Sincerely, concerning that I did not realize microspheres only based PMMA because these different fractions were object of other works already realized in our laboratory and there is not enough product for encapsulate the HCTZ only with the PMMA and if we re-synthesize the PMMA I will not have the same masses to make the comparison. For the microparticles containing EC and β-CD (Fig.1-7), we confirm by optical microscopy that the surface of microspheres contains smaller microspheres and not powders of drug.

**Question: 10**

The added sentence: "In fact, the SEM provided photographs of microparticles composed only of ethyl cellulose (Fig.1-1)… «Should be reorganize since SEM analysis provided photos of all microspheres, not only of EC. The explanation: "The diffusion rate of solvent is too fast and the solvent may diffuse into the aqueous phase before stable microparticles are developed and formed, causing the aggregation of microparticle preparation" is not clear to me and need to be revised. It is known that DCM and water solutions are not miscible, therefore is less possible that DCM would diffuse to water. But DCM is highly volatile solvent and tends to evaporate very fast which could be a reason of particle aggregation.

**Answer 10**

The first sentence apply

DCM effectively forms an emulsion with the aqueous phase containing the PVA and its rapid evaporation rate not allowing the formation of stable microparticles and develops this form, subsequently causing the aggregation of the preparation of microparticles and consequently, the undissolved polymer produced irregular and rod shaped particles.

**Question: 10**

In the part of XRD analysis, the authors discussed about the interactions between drug and polymer matrix but they did not point out whether the appearance of HCTZ characteristic peaks proved that the drug is in crystalline form or not.

**Answer 10:**

The crystalline form of HCTZ is reduced by the decrease in peak intensity and the disappearance of some. So we can only say that the HCTZ became semi crystalline (Apply in article)

**Question: 11**

From the revised FTIR spectra of drug encapsulated microspheres, still the most dominant were the peaks coming from EC polymer due to a higher content in blends. Also, in the FTIR spectra, in the drug encapsulated microspheres, there is no visible peaks inherent to drug, maybe only in the area from 500 to 1000 cm-1, especially there is no characteristic peak coming from N-H vibrations. It is strongly recommended to authors to better analyse FTIR spectrum of the microspheres and to revise the following part: "The spectra of HCTZ delayed release formulations show a most of peaks of drug were present and broad peak at the same place of the peak observed at the spectrum of pure drug, which indicates that the spectra of the HCTZ loaded microspheres appear as the sum of the spectra of pure HCTZ and polymers... "

**Answer 11:**

The FTIR spectra were redone a second time and the characteristic peaks of the N-H function become more legible (apply in article)

The improvement of the spectrum has confirmed what has been written in the following sentence “The spectra of HCTZ delayed release formulations show a most of peaks of drug were present and broad peak at the same place of the peak observed at the spectrum of pure drug, which indicates that the spectra of the HCTZ loaded microspheres appear as the sum of the spectra of pure HCTZ and polymers... "

**Question 12:**

 In the revised manuscript, there is again an opposite assertion; according to FTIR analysis there were no physical or chemical interactions between polymers and drug and from XRD analysis, authors concluded that there was an interaction between HCTZ and EC. Please, try to distinguish this.

**Answer 12:**

In the DRX part, I meant that the disappearance and displacement of some peaks of HCTZ show the reduction of its crystalline form and not of a physical or chemical interaction. For this the correction is made in the article

**Question 13:**

Analyzing the literature in the part of In vitro dissolution of HCTZ... the authors commented that dissolution rate of drug could be improved by the interaction between polymer matrix and drug. Does the authors want to point out that drug is encapsulated in an amorphous form since they cited "However, amorphous drugs do not need such energy41 and this enhancement also might be attributed to the increase in the wettability and solubility of the drug42"? In addition, the sentence "Loyd et al. and Pokharkar et al. demonstrated that the improvement in the dissolution rate of drug may be due to the enhancement of the physical amorphism of the latter38, 39" is not clear to me and need to be revised. What is the physical amorphism of latter?

**Answer 13:**

the sentence "However, amorphous drugs do not need such energy41 and this enhancement also might be attributed to the increase in the wettability and solubility of the drug42" is general and does not confirm that our drug is amorphous but explains the improvement of the dissolution of our drug by the reduction of its crystallinity already confirmed in the DRX spectra

the sentence "Loyd et al. and Pokharkar et al. demonstrated that the improvement in the dissolution rate of drug may be due to the enhancement of the physical amorphism of the latter38, 39" is corrected in article

**Question 14:**

The resolution of the drug release profiles photos is not satisfactory and the Figure 4 and Figure 5 require revision. Also, title of the Table III should be revised (Drug release kinetics of HCTZ after...).

**Answer 14:** Apply in article

**Question 15:**

In the section of mathematical models, the word "milieu" has no meaning ("Thus, the values of the Higuchi’s dissolution constant in the intestinal milieu are relatively high…). Please, correct it.

**Answer 15:**

We have corrected the Higuchi’s dissolutions constants in the two medium because they were not compatible with the experimental points given in the figures 4 and 5.

**Question 16:**

The sentence: «For this several formulations are prepared by a solvent evaporation method with selected polymers." in the Conclusion part has no sence and is not gramatically correct. Please, revise it. After the authors revise their answer to the question 11, they are supposed to reorganize the sentence: "The microspheres prepared are characterized by Fourier transform infrared spectroscopy (FTIR) analysis and X-Ray diffraction (XRD) studies indicating that there is no interaction between drug and polymers." In the Conclusion section, L5 formulation need to be specifies.

**Answer 16:** apply in article

**Question 17:**

The 13C NMR spectrum has no desirable quality and only CDCl3 characteristic peaks could be visible. Therefore, it is quite difficult to estimate the structure of PMMA fractions. The authors should provide better spectra.

**Answer 17:**

I am sending you the enhanced 13C NMR spectrum