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# COMPATIBILITY STUDIES OF OLANZAPINE (API) WITH PLGA 750S POLYMER

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**ABSTRACT**

The microspheres were characterized by in-vitro dissolution and other Physiochemical methods. A simulation of multiple dosing at weekly or 15 -day regimen revealed pulsatile behavior for all formulations with steady state may be achieved by the second dose. The current studies was design and evaluate biodegradable PLGA microspheres for sustained or extended release, with primary goal of avoiding combination of oral therapy for the treatment of schizophrenia. PLGA copolymers 75:25 was used to prepare four microsphere formulations of anti-psychotic drug Olanzapine. Overall, the in-vitro study of Formulations 001, 002, 003, or 004 will eliminate the need for combination oral therapy and reduce time to achieve steady state, with a smaller washout period upon duration of therapy. Results of this study prove the suitability of using PLGA 75:25 copolymers of different composition and molecular weight to produce sustained or extended release formulations that can enhance pharmacological effectiveness for anti-psychotic intra-muscular administration of Olanzapine.

***Keywords: sustained release, PLGA microspheres, Olanzapine***

## INTRODUCTION

With high patient compliance, microspheres are now regarded as a dependable and efficient release mechanism that lowers doses, frequency of dosing, and the risk of dosage dumping (2). For example, polyesters employed in microspheres have the advantage of employing water as a vehicle to generate suspensions which allows consistent release of desired medicine. Microspheres prepared by natural or synthetic polymers provides sustained release. It has been established that a medication's physicochemical characteristics, main burst, and excipients all have a direct impact on how quickly the drug leaves the microsphere[3].Injectable microsphere systems were developed in late 70's. Poly (lactide) and/or poly (lactide-co-glycolide) was used to encapsulate an ester of norethisteron calledNET via oil-in-water emulsion/solvent evaporation process. These microcrystals ofNET were encapsulated into microspheres of PLA and PLGA. Since then PLGA has been the first choice of polymer for preparation of microspheres to encapsulateAPIs using w/o or o/w emulsion/solvent evaporation technique. Poly (ε-caprolactone)

is the secondly most accepted polymer for preparation of microspheres to encapsulate APIs. Moreover PLGA, PCL and PLA, diblock copolymers of lactide, ethylene glycol, L-lactide and ε-caprolactone, triblock co polymers of caprolactons, lactides and glycolides, have also been used to encapsulate APIs via o/w emulsion / solvent evaporation. [3]The composition of the microspheres and the rate at which they degrade have an impact on the release profiles of the API. For instance, the hydrolytic breakdown rate of PGA, PLA, and PCL is in the following order: PGA > PLA >> PCL. In contrast to PLA and PGA, which had inferior permeability in the case of steroidal pharmaceuticals but showed uniform biodegradation, PCL has great permeability in the case of steroidal medications but exhibits sluggish biodegradation. When the system's hydrophilic glycolide component is increased, it has been found that PLGA microspheres breakdown more quickly and release API more quickly. The release patterns of API are further influenced by the polymer's chirality, density of cross-linking, and loading of medicines in microspheres. When the amount of cross-linking is greatly increased, it causes an increase in the barrier density for drug diffusion and a slower release of the API in casein and chitosan microspheres. When unencapsulated medication is more readily available on the surface of microspheres in greater quantities, there is a higher initial burst in microspheres. [3]

## Materials and Methods

### Compatibility of API with polymer:

Compatibility of Olanzapine and polymer PLGA was tested on followingparameters.

### FTIR Analysis:

FTIR analysis of physical mixture of olanzapine and PLGA was performed onPerkin Elmer FTIR spectrometer.

### DSC analysis of physical mixture of Olanzapine andPLGA

DSC analysis of physical mixture of olanzapine and PLGA was performed on Mettler Toredo which is shown below figure 5.6 Approximately 2 mg of API and polymer mixture was weighed in standard aluminum sample holder. In first cycle the temperature sample holder was brought to -10˚C. Then the temperature of sample holder was raised at the rate of 10 ˚C per minute up to 60˚C. In the Second cycle the temperature sample holder was decreased to -10˚C at rate of 10 ˚C per minute. In third cycle temperature of sample holder again raised from -10˚C up to 100˚C at rate of 10˚C per minute. Air flow of 50mL per Minute was maintained throughout the experiment.

**RESULT & DISCUSSION**

### Compatibility of olanzapine (API) with PLGA 750S polymer

## FTIR analysis of physical mixture

The physical mixing of olanzapine and PLGA revealed 17 peaks in the FTIR analysis that are characteristic of PLGA and olanzapine. Peak at 2843.95 cm-1 is dedicated to CH2, CH3, and asymmetric stretching; peak at 1587.57 cm-1, 1220.17 cm-1 for C=N stretching, 1005.75 cm-1 for aromatic ring deformation, and peak at 971.65 cm-1 for C-S stretching are characteristic of Olanzapine; and peak at 2843.95 cm-1 is dedicated to C=O stretching; these are the characteristics of PLGA and PLGA, respectively. The FTIR demonstrates that the physical mixture of API and polymer does not exhibit any chemical reactions, proving their compatibility.

**Table 6.5 : FTIR Interpretation for physical mixture of olanzapine and PLGApolymer**

| Sr. | Wave Number | Interpretation |
|---|---|---|
| 1 | 2843.95 | $CH_2$, $CH_3$, $CH_2$ asymmetric stretching |
| 2 | 1751.67 | C=O stretching |
| 3 | 1587.57 | C-N stretching |
| 4 | 1560.61 | C-N stretching |
| 5 | 1455.61 | $CH_2$ deformation |
| 6 | 1420.14 | $CH_3$ deformation |
| 7 | 1364.98 | $CH_2$ wagging |
| 8 | 1284.69 | $CH_2$ twisting |
| 9 | 1269.79 | $CH_2$ twisting |
| 10 | 1220.17 | C=N stretching |
| 11 | 1180.29 | C-H deformation |
| 12 | 1138.02 | Aromatic ring stretching CH deformation |
| 13 | 1086.22 | C-O stretching |
| 14 | 1044.44 | Aromatic ring stretching C-H deformation |
| 15 | 1005.75 | Aromatic ring deformation |

| | | |
|---|---|---|
| 16 | 971.65 | C-S stretching |
| 17 | 851.79 | C-H out of plane banding |
| 18 | 757.62 | C-H out of plane deformation |
| 19 | 711.31 | Aromatic ring deformation |

## DSC analysis of physical mixture of olanzapine and PLGA Polymer 750S

Using the same set of conditions used for the DSC study of Polymer PLGA 750S, the glass transition temperature for the PLGA and Olanzapine mixture was established on Mettler Toledo equipment. Researchers discovered that the glass transition started at 49.44 C and reached its end point at 51.48 C. Olanzapine produces a physical combination without undergoing any chemical reactions, as shown by a comparison with the DSC thermogram of pure polymer PLGA 750S. Also, it is evident from the mixture's DSC that there was no thermal decomposition or chemical reaction in the physical mixture (glass transition temperature of pure PLGA was 48.69 C).

**Figure 6.3: DSC Thermogram of physical mixture of olanzapine and PLGAPolymer 750S**

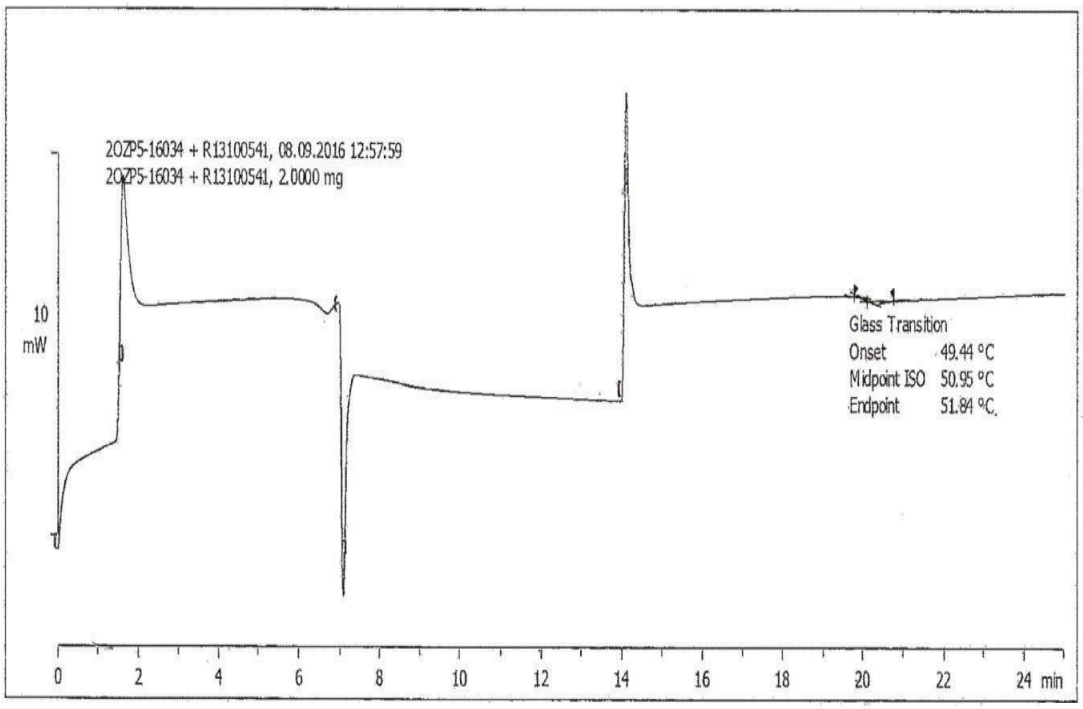


Figure 6.3 : DSC Thermogram of physical mixture of olanzapine and PLGA Polymer 750S

## CONCLUSIONS

Olanzapine is a second-generation analytical antipsychotic medication. It is used to treat mild to severe mania associated with bipolar illnesses as well as schizophrenia. The principal oral dose, which can be given as a single therapeutic agent or as part of a combination therapy, is 10 mg per day. Degradation of PLGA depends on percentage of glycolic monomer in polymer. Higher the quality of glycolic acid lower is the time for degradation. Hence PLGA with 75:25 lactic acid : Glycolic acid ratio will take higher time for degradation in comparison to 50:50 lactic acid to glycolic acid ratio. Keeping in mind required properties of polymer PLGA 755 (lactic acid: Glycolic 75:25) was selected in present study to prepare microsphere of olanzapine.

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