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Research Article

# COMPARATIVE STUDY OF DIFFERENT SURFACTANTS FOR SOLUBILITY ENHANCEMENT OF TWO CLASS II DRUGS FOR TYPE II DIABETES MELLITUS

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**ABSTRACT**

The Objective of the study is to compare the solubilising efficiency of five different surfactants represented by Sodium Lauryl Sulphate, Tween 80, Polyethylene Glycol 6000, Cremophor RH40, Poloxamer 407 to develop a stable immediate release solid oral dosage form. Pioglitazone Hydrochloride and Glimepiride are class II (low solubility, high permeability) antidiabetic drugs used in the treatment of type II Diabetes mellitus (NIDDM). Immediate release tablets were prepared by wet granulation method in which the surfactants were added by dissolving it in binder solution. Compatibility study was carried out and was found that there was no interaction between the ingredients. The formulated tablets were then evaluated for hardness, friability, disintegration time and dissolution by HPLC. Stability studies were also carried out for 3 months. From the above study it was found that among the five surfactants used, Poloxamer 407 showed better dissolution and also resulted in a stable dosage form.

**Keywords:** Pioglitazone, Glimepiride, Poloxamer 407, Surfactants, Solubility.

## INTRODUCTION

Pioglitazone Hydrochloride is an oral Anti-diabetic agent that acts primarily by decreasing insulin resistance. It is used in the management of type-2 Diabetes mellitus (also known as Non-Insulin-Dependent Diabetes mellitus [NIDDM] or adult-onset Diabetes). Glimepiride is an oral blood-glucose-lowering drug of the sulfonylurea class.

Both Pioglitazone and Glimepiride act complimentary to each other; since Pioglitazone is an insulin sensitizer and decreases insulin resistance at the periphery and in the liver; without stimulating insulin secretion, thereby exerting antihyperglycemic effect[1]. Glimepiride, a sulphonylurea class drug which increases insulin secretion.

The time course of action of both the drugs i.e. Pioglitazone and Glimepiride fall in same range as the pharmacokinetic parameters. Hence, Pioglitazone and Glimepiride complement each other's action pharmacokinetically also [2].

It is found that there is a significant decrease in the (<0.05) mean fasting blood triglyceride levels with addition of Pioglitazone sulphonylurea therapy. Both Pioglitazone and Glimepiride are recommended as once daily therapy.

Once a day regimen would support the combination along with reduced dose of each drug and will have better patient compliance. Therefore, it is appropriate to combine Pioglitazone and Glimepiride as fixed dose combination[3].

The main objective of this work is to compare the solubilising efficiency of five different surfactants to enhance the solubility of class II (low solubility high permeability) drugs [4,5].

## MATERIALS AND METHODS

### Drug Excipient Compatibility Study

Suitable excipients were selected and mixed with the drug and were sifted through 40# mesh, triturated well using mortar and pestle until homogenously mixed. Then sufficient quantity of the mixture was packed in LDPE bags and glass vials, placed at 40°C/75% RH and 60°C respectively. The samples were checked for their physical and chemical changes. The glass vials at 60°C were analysed at second week and the LDPE bags at 40°C/75% RH were analysed at second and fourth week.

The results showed that there was no interaction between the drug and the excipients used in the formulation.

**Table 1: Formulation of Tablets**

| S.N o | Ingredients | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| 1. | Pioglitazone HCl | 16.55 | 16.55 | 16.55 | 16.55 | 11.82 |
| 2. | Glimepiride | 2.00 | 2.00 | 2.00 | 2.00 | 1.43 |
| 3. | Lactose Monohydrate | 84.17 | 82.11 | 82.11 | 79.76 | 53.96 |
| 4. | Sodium Lauryl Sulphate | 1.20 | - | - | - | - |
| 5. | Sodium Starch Glycolate | 4.80 | - | - | - | - |
| 6. | PVP K30 | 3.60 | 5.60 | 5.60 | 5.60 | 4.29 |
| 7. | Starch 1500 | - | 9.8 | 9.8 | 9.8 | 10.71 |
| 8. | Tween 80 | - | 1.12 | - | - | - |
| 9. | PEG 6000 | - | - | - | 3.47 | - |
| 10. | Poloxamer 407 | - | - | - | - | 1.79 |
| 11. | Purified water | Q.S | Q.S | Q.S | Q.S | Q.S |
| 12. | Starch 1500 | - | 11.32 | 11.32 | 11.32 | 7.14 |
| 13. | Magnesium Stearate | 0.48 | 1.00 | 1.00 | 1.00 | 0.36 |
| 14. | MicrocrystallineCellulose 102 | 7.20 | - | - | - | - |
| 15. | Acdisol | - | I 4.20 | 4.20 | 4.20 | 3.57 |
| | | - | E 5.60 | 5.60 | 5.60 | 4.29 |
| 16. | Aerosil | - | I 0.28 | 0.28 | 0.28 | 0.21 |
| | | - | E 0.42 | 0.42 | 0.41 | 0.29 |
| 17. | Cremophor RH 40 | - | - | 1.12 | - | - |
| 18. | Iron Oxide Yellow | - | - | - | - | 0.14 |

**Manufacturing Process** [6-9]

The active and Intragranular (I) ingredients were weighed and sifted through #40 mesh and the colorant (Iron oxide yellow) sifted using #100 mesh. Binder solution was prepared by dissolving the surfactant and then Povidone K30 in purified water. It was then granulated with the binder solution, dried at 60°C in tray drier and checked for LOD (NMT 2.0%). The dried granules were passed through #30 mesh and retains were milled using multimill fit with 1.0 mm mesh. The extragranular (E) ingredients were weighed, sifted and blended with the dried granules for ten minutes. The lubricant was sifted through #60 mesh and blended with the same for 3 minutes.

The blend was compressed using 7.1 FFBE punches. (Table 1).

**Evaluation of Formulated Tablets** [6, 8,10-12]

The formulated tablets were evaluated for Average Weight, Thickness, Hardness, Friability, Disintegration, Moisture content, Dissolution and Related Substances by HPLC and Assay (Table 2).

**Table 2: Evaluation of Formulated Tablets**

| Sl.No. | Parameters | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| 1. | Average weight (mg) | 120 | 140 | 140 | 140 | 140 |
| 2. | Thickness (mm) | 2.9-3.1 | 4-5.6 | 4.3-5.1 | 3.5-4.6 | 2.72- 2.74 |
| 3. | Hardness ($k_p$) | 7-8 | 3.2-3.8 | 3.2-3.31 | 3.24-3.35 | 4-5 |
| 4. | Friability (% w/w) | 0.01 | 2.54 | 0.11 | 0.14 | 0.3 |
| 5. | Disintegration time (minutes) | 4.55 | 0.06 | 3.52 | 8.20 | 4.55 |
| 6. | Dissolution | pH 2.1 simulated Gastric fluid, 900ml, Apparatus II, 75rpm at 45 minutes | | | | |
| | Pioglitazone | 98.80 | Initial | 96.1 | 99.2 | 99.1 | 99.8 |
| | | | 1M | 95.0 | 95.1 | 97.0 | 99.8 |
| | | | 2M | 94.2 | 93.9 | 95.6 | 99.0 |
| | | | 3M | 93.0 | 93.0 | 93.2 | 98.6 |
| | Glimepiride | 87.30 | Initial | 96.4 | 99.1 | 93.6 | 98.2 |
| | | | 1M | 89.9 | 91.3 | 92.6 | 98.1 |
| | | | 2M | 86.9 | 74.2 | 90.3 | 98.0 |
| | | | 3M | 82.1 | 70.1 | 86.9 | 97.8 |

**RESULTS AND DISCUSSION**

Immediate release tablets of Pioglitazone (15mg) and Glimepiride (1mg, 2mg) tablets were prepared. Preformulation studies were conducted and it was found that the excipients were compatible. The solubility of both the poorly soluble drugs [Pioglitazone and Glimepiride] was enhanced using different surfactants and trial using Poloxamer gave satisfactory results when compared with other surfactants. *In-vitro* Dissolution studies for the tablets were conducted using pH 2.1 Simulated Gastric Fluid solution as the dissolution medium. Assay for the prepared tablets were carried out and the results were found to be satisfactory. Accelerated Stability study of the tablets was found to be satisfactory. No sign of degradation was observed in HPLC analysis.

Solubility enhancement of poorly soluble drugs can be achieved by using surfactants. In the present work, solubility was enhanced using Poloxamer and it showed better dissolution profiling which is comparable with other formulation. Therefore, Poloxamer 407 was found to increase solubility of Piglitazone & Glimepiride (Fig. 1 & Fig. 2).

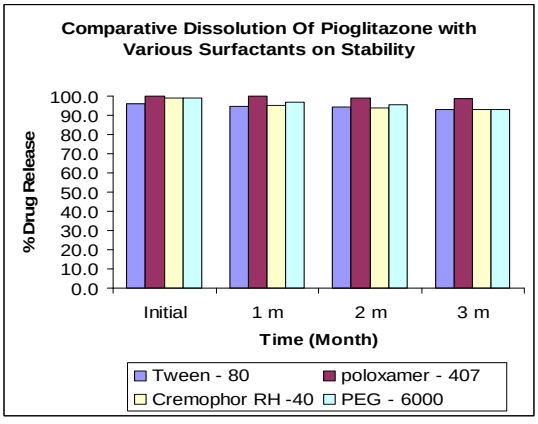


**Fig. 1: Comparative Dissolution of Pioglitaz one with various surfactants on stability**

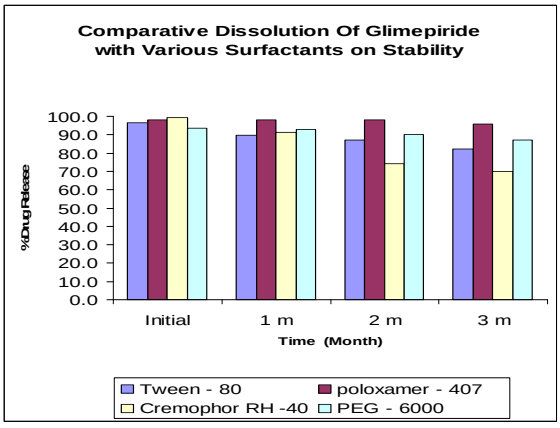


**Fig. 2: Comparative Dissolution of Glimepiride with various surfactants on stability**

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