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Gliclazide Extended Release dosage form of Anti-diabetic Drugs : A Review

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Abstract : In the present day many research did on extended release formulation. Different type of drug release mechanism used to formulate extended release tablets like matrix, Hot melt granulation, and pellet technology are used for gliclazide investigation. Gliclazide come under the sulphonyureaclass of anti- diabetic drugs. An extended release dosage form help in reduce the undesirable effects that may occur by peak effect of drugs. It helps to maintain the drug concentration in blood. Very analytical validation was done for made the extended release dosage form of gliclazide like preformulation studies, formulation and evaluation , stability studies, bioequivalence studies etc.

Keywords : Extended Release, Gliclazide, Organoleptic, Diabetes mellitus.

INTRODUCTION:

Extended release drug delivery system helps us to maintain the therapeutic level of drug. This drug delivery system helps in solving the problem regarding to delivering of drug to their specific targeted organ. For developing the oral extended drug delivery drugs matrix system used by us. The main goal of this drug delivery system to maintain steady state of drug. Gliclazide used in diabetes mellitus. It is an anti-hyperglycemic agent. Most of the oral controlled drugs followed first order and second order of drug release. Fick's first law of diffusion used to determined the rate of drug release and fick's second law, drug accumulation speed determined by using drug diffusivity and curvature of drug concentration. Various technologies are used for extended release drug delivery system like matrix technology, hot melt granulation technology and multiparticulate technology. By literature search on extended release tablets various technologies has been elaborated in coninution. Formulation of gliclazide official mentioned in pharmacopeia for estimation of gliclazide extended release tablets made by these three technologies: matrix technology, hot melt granulation technology and multiparticulate unit dose technology. By using UV spectrophotometric method assay and dissolution profile was estimated at 226nm and 290nm. By using X ray diffraction, XRD pattern of control sample and exposed sample were studied and obtained pattern overlaid to check any incompatibility.

Matrix technology

Various polymers are used for gliclazide extended release tablets by matrix technology such as Polyethylene oxide, Xanthan gum, Chitosan sodium alginate and copolymers of Povidone, Polyvinyl alcohol and hydroxyproplymethyl cellulose. Wet granulation method are used for preparation. Different parameters like sieve analysis, Assay, Blend uniformity with their specification limits are considered. Different methods was included slugging/ deslugging as the wet granulation method for preparation of tablets. Polyethylene oxide used as rate controlling polymer. For kept stability formulation was packed in Alu/Alu blisters. Xanthum also used in ER tablet formulation as rate controlling polymer. By the combination of HPMC K4M and HPMC K100 LV compared the dissolution profile with Diamicron MR Tablet.

Hot melt granulation technology

To formulate gliclazide extended release tablets by using hot melt granulation technique. Polyethylene glycol 8000 and Hydroxypropylmethylcellulose are used to get desired result. Various factors like melted mass temperature, granulation time, Time for hardness off tablets.

Multiparticulate unit dose technology

Different process occurred in multiparticulate unit dose technology by making gliclazide immediate release pellets, coating of the pellets, blending with lubricants and diluents in end compression of tablet. All packaging material select on the basis of specifications. On different storage conditions samples were withdrawn periodically and analyzed for physical and chemical stability. To obtain formulation which gives the drug release profile similar to innovator was done by systemic study. Different input variables were studied

(i) For coating of the pellets definite composition of coating material were used to achieve desired drug profile

(ii) Due to rupture of the coating pellets were effect the drug release

For evaluation of gliclazide extended release tablets following parameters were evaluated

- **Blend analysis :** Loss on drying, bulk density, tapped density, compressibility index, hausner's ratio and sieve analysis was analysed in blend
- **In – process parameters :** Loss on drying of the tablets was measured using hardness, thickness and friability these following parameters were evaluated
- **Description :** For their physical appearance and colour tablets were checked
- **Drug content :** By UV spectrophotometer drug content was determined
- **In – vitro dissolution profile :** By using dissolution apparatus at 50 rpm in – vitro drug release was carrie out. pH 4.5 acetate buffer and ph 7.4 buffer was used for multimedia dissolution.. pH- 6.8 phosphate buffer was used as the dissolution medium. Samples were withdrawn at various time points and analyzed by UV spectrophotometry
- **Related substances :** By using HPLC related substances were determined
- **Content uniformity :** The drug content was determined in 10 individual tablets by UV spectrophotometry

PVC/PVDC/ Alu blisters, Alu/Alu blisters and HDPE Bottles were used for optimized formulation packing. All the packaging materials were selected as per specification. The integrity of the blisters checking by blister vacuum leakage test. At different storage condition samples were withdrawn periodically and analyzed for physical and

chemical stability. Visual appearance, assay, dissolution profile, hardness, average weight and related substances all these parameters were evaluated.

Bioequivalence study

Followed ICMR guidelines, schedule Y 2005 of Drug and cosmetic act, India, the World Medical Association Declaration of Helsinki, Good Clinical Practice (GCP). Advancment in the field of pharmaceutical manufacturing and achieve better therapeutic value to modified release dosage forms has create pressure on consumer and manufacturer that to strike balance.

Clinical pharmacology of Gliclazide

Gliclazide is a sulphonylurea drug with half life of around 11 hours. It is broadly metabolized and renal clearance accounts for only 4% of total drug clearance. It contain azabicyclo – octyl group which confer special properties on the basic sulphonylurea moiety. Gliclazide stimulates insulin secretion all the way through the beta cell sulphonylurea receptor and through a direct effect on intracellular calcium transport. In type 2 diabetes, it specifically improves the abnormal first phase insulin release and also has an effect on the second phase. This pattern of insulin release is thought to elucidate the lower incidence of hypoglycemic episodes and weight gain compared with some other sulphonylureas. It is also reduced in hepatic glucose production and improvement in glucose clearance, without changes in insulin receptors. This suggest a possible post – receptor effect on insulin receptors. This also suggests a possible post – receptor effect on insulin action, perhaps by stimulation of hepatic fructose- 2, 6- bisphosphate and muscle glycogen synthase. Gliclazide reduce platelet adhesion, aggregation and hyperactivity and increases fibrinolysis. These actions, thought to be independent of its hypoglycemic activity may make gliclazide useful in halting the progression of diabetic microangiopathy.

Present scenario of gliclazde

Servier Canada first is patented the gliclazide and the drug was approved for therapeutic purpose in the name of Diamicron MR tab. Release pattern of formulation is very slow and and long processed. So many approaches had been taken to overcome such problems. Formulations had been developed in the form of matrix tablets , sustained release , immediate release, bilayer tablets. Encapsulation and microcapsulation techniques has also been tried. Lastly It is reported that Disphar International B.V.7255 PZ Hengelo (NL) has patented Sustained-release formulation of gliclazide on 05-05-2010,where Inventorship was recorded in the name of Wit, Johannes Bernardus, Maria & 3742 ZD Baarn (NL) Doshi, Hitesh kumar Anilkant Mulund (W), Mumbai 400 080 (IN) (EP 2 181 705 A1).

Conclusion

The purpose of this review is to collect information of gliclazide XR about its formulation and pharmacology. Gliclazide fastly absorbed in all species with a plasma peak observed between 1 and 6 hours. Recent analytical techniques has been developed to detect and quantify gliclazide for in vivo studies with optimum retention time. The hydrophilic matrix of hypromellose-based polymer in the novel formulation effects a progressive release of the drug which parallels the 24-hour glycaemic profile in **untreated patients with type 2 diabetes mellitus**.

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