WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

SJIF Impact Factor 7.421

Volume 8, Issue 4, 1236-1245 Research Article ISSN 2278 – 4357

PREPARATION AND EVALUATION OF STARCH - PEG 1500 CO-PROCESSED EXCIPIENT AS A NEW DIRECTLY COMPRESSIBLE VEHICLE IN TABLET FORMULATIONS

B. Lakshmi Satya[1] and K. P. R. Chowdary[2]*

[1]Vishnu Institute of Pharmaceutical Education and Research, Vishnupur, Narsapur, Medak 502313.

[2]Vikas Institute of Pharmaceutical Sciences, Near Airport, Nidigatla Road, Rajahmundry 533105.

Article Received on
12 Feb. 2019,

Revised on 04 Mar. 2019,
Accepted on 25 Mar. 2019

DOI: 10.20959/wjpps20194-13507

***Corresponding Author**
Prof. K. P. R. Chowdary
Vikas Institute of Pharmaceutical Sciences, Near Airport, Nidigatla Road, Rajahmundry 533105.

ABSTRACT

An efficient platform for the manipulation of excipient functionality is provided by co-processing two or more existing excipients. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvements as well as masking the undesirable properties of individual excipients. The objective of the present study is to prepare and characterize starch - polyethylene glycol 1500 (Starch-PEG) co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. Starch-PEG co-processed excipient was prepared by gelatinizing potato starch in the presence of PEG 1500 and drying the resulting mass and was characterized by determining melting point, solubility, swelling index in water, pH, and micromeritic characters namely particle size, bulk density, tapped density, angle of repose and compressibility index and evaluated for its application as directly compressible vehicle in tablet formulations. Starch-PEG co-processed excipient prepared was found to be granular, discrete and free flowing. It is insoluble in water and aqueous fluids of pH 1.2, 4.5 and 7.4. It exhibited high swelling (445%) in water. Starch-PEG co-processed excipient has excellent flow properties alone and as blends with selected drugs it exhibited excellent to good flow properties. Tablets of (i) aceclofenac and (ii) ibuprofen prepared by direct compression method employing Starch-PEG co-processed excipient as DCV were of good quality with regard to drug content, hardness, friability and disintegration time. All the tablets

formulated employing Starch-PEG co-processed excipient disintegrated rapidly within 15 seconds. With both the two drugs, the tablets prepared gave rapid dissolution of the contained drug. Dissolution was complete with in 15-20 min in all the cases and fulfilled the official (I.P 2010) dissolution rate test specification prescribed in each case. Thus Starch-PEG co-processed excipient developed in this study was found to be a promising directly compressible vehicle for the preparation of compressed tablets with fast dissolution characteristics.

KEYWORDS: Co- processed Excipient, Starch- Polyethylene glycol 1500 Co- processed Excipient, Directly compressible vehicle, Aceclofenac, Ibuprofen, Direct Compression.

INTRODUCTION

An efficient platform for the manipulation of excipient functionality is provided by co-processing two or more existing excipients. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvements as well as masking the undesirable properties of individual excipients.[1] The availability of a large number of excipients for co-processing ensures numerous possibilities to produce tailor-made "designer excipients" to address specific functionality requirements. Co-processed excipients are prepared by incorporating one excipient into the particle structure of another excipient using processes such as co-drying. Co-processing of excipients in the pharmaceutical industry can be dated back to the late 1980's with the introduction of co-processed microcrystalline cellulose and calcium carbonate[2], followed by Cellactose (Meggle Corp.,Wasserburg, Germany) in 1990, which is a co-processed combination of cellulose and lactose. A similar principle was applied in developing silicified microcrystalline cellulose (Prosolve), which is the most widely used co-processed excipient.[3] The objective of the present study is to prepare and characterize Starch – Polyethyleneglycol (Starch-PEG) co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. Starch-PEG co- processed excipient was prepared by gelatinizing potato starch in the presence of polyethylene glycol – 1500 and drying the resulting mass.

EXPERIMENTAL

MATERIALS

Aceclofenac and ibuprofen were gift samples from M/s Natco Laboratories Ltd., Hyderabad. Potato starch, PEG 1500, Crospovidone, talc and magnesium stearate were procured from commercial sources. All other materials used were of Pharmacopoeial grade.

Afenak100 tablets of Ranbaxy Laboratories Ltd., New Delhi ; Batch No. 9743788; Mfg. Date: April/2011; Exp. Date: March/2013 and Brufen 400 tablets of Abbott India Ltd., Goa; Batch No. 96809D7; Mfg. Date: 11/2010; Exp. Date: 10/2013 were procured from local market.

METHODS

Preparation of Starch-PEG Co-processed Excipient

Potato starch (9 g) was dispersed in 20 ml of water to form smooth slurry. PEG 1500 (1 g) was dissolved in purified water (40 ml) and the solution was taken in a separate beaker and heated to boiling. Starch slurry was added to boiling solution while stirring. Stirring while heating was continued for 15 to 20 minutes to form a thick mass. The mass was dehydrated by the addition of acetone (20 ml) and mixing. The product formed was collected by decantation and dried at 80^{o}C for 4 hours. The dried product was grinded and sized to obtain -20+100 mesh sized particles.

Characterization of Starch-PEG Co-processed Excipient

Starch-PEG co-processed excipient prepared was characterized by determining melting point, solubility, swelling index in water, pH, and micromeritic characters namely particle size, bulk density, tapped density, angle of repose and compressibility index.

Solubility

Solubility of Starch-PEG was tested in water, aqueous buffers of pH 1.2, 4.5, and 7.4.

pH

The pH of a 1% w/v slurry was measured.

Melting point

Melting point was determined by using melting point apparatus.

Swelling Index[4]

Starch-PEG (0.5 g) was added to 10 ml of water and petroleum ether taken in two different graduated test tubes and mixed. The dispersion in the tubes was allowed to stand for 24 hrs. The volumes of the sediment in the tubes were recorded. The swelling index of the material was calculated as follows.

S.I (%) = (Volume of sediment in water – Volume of sediment in petroleum ether)/ (Volume of sediment in petroleum ether)

Particle size

Particle size analysis was done by sieving using standard sieves.

Bulk density[5]

Bulk density (g/cc) was determined by three tap method in graduated cylinder.

Angle of repose[6]

Angle of repose was measured by fixed funnel method.

Compressibility index[7]

Compressibility index (CI) was determined by measuring the initial volume (V_0) and final volume (V) after hundred tappings of a sample of the product in a measuring cylinder.

CI was calculated using equation,

Compressibility index (CI) = $[(V_0\text{-}V)/V_0] \times 100$

Estimation of Aceclofenac

An UV Spectrophotometric method based on the measurement of absorbance at 275 nm in phosphate buffer of pH 6.8 was used for the estimation of aceclofenac. The method was validated for linearity, accuracy, precision and interference. The method obeyed Beer's law in the concentration range of 1 – 10 µg/ ml. When a standard drug solution was repeatedly assayed (n=6), the relative error and coefficient of variance were found to be 0.65 % and 1.45 % respectively. No interference by the excipients used in the study was observed.

Estimation of Ibuprofen

An UV Spectrophotometric method based on the measurement of absorbance at 221 nm in phosphate buffer of pH 7.2 was used for the estimation of ibuprofen. The method was validated for linearity, accuracy, precision and interference. The method obeyed Beer's law

in the concentration range of 1 – 10 µg/ ml. When a standard drug solution was repeatedly assayed (n=6), the relative error and coefficient of variance were found to be 0.85 % and 1.15 % respectively. No interference by the excipients used in the study was observed.

Preparation of Tablets by Direct Compression Method

Tablets of (i) aceclofenac (50 mg) and (ii) ibuprofen (50 mg) were prepared by direct compression method as per the formulae given in the Table 2 employing Starch-PEG co-processed excipient as directly compressible vehicle. All the materials required as per the formula were blended in a closed polyethylene bag. The blends were compressed into tablets on a 10 station tablet punching machine (Rimek) to a hardness of 6 kg/cm^2 using 9 mm flat punches.

Evaluation of Tablets

All the tablets prepared were evaluated for content of active ingredient, hardness, friability, disintegration time and dissolution rate. Hardness of tablets was tested using Monsanto hardness tester. Friability of the tablets was determined in a Roche Friabilator. Disintegration time was determined in a Lab India tablet disintegration test machine (model: DT 1000) using water as test fluid.

Estimation of Drug Content in the Tablets

From each batch of tablets prepared 10 tablets were accurately weighed and powdered. Tablet powder equivalent to 50 mg of drug was taken for assay into a 100 ml conical flask and extracted with 3×20 ml quantities of methanol. The methanolic extracts were filtered and collected into a 100 ml volumetric flask and the volume was then made up to 100 ml with methanol. The solution was then suitably diluted with phosphate buffer of pH 6.8 in the case of aceclofenac; with phosphate buffer of pH 7.2 in the case of ibuprofen. The absorbance of the solutions was measured at 275 nm in the case of aceclofenac and at 221 nm in the case of ibuprofen. Drug content of the tablets was calculated using the standard calibration curve in each case.

Dissolution Rate Study

Dissolution rate of the tablets prepared was studied employing USP 8 station Dissolution Rate Test Apparatus (M/s Labindia Disso 8000) with a paddle stirrer at 50 rpm. Phosphate buffer of pH 6.8 (900 ml) and phosphate buffer of pH 7.2 (900 ml) were used as dissolution fluids for aceclofenac and ibuprofen respectively. One tablet was used in each test. A

temperature 37±1^{0}C was maintained throughout. Samples of dissolution medium (5 ml) were withdrawn through a filter (0.45 µ) at different time intervals and assayed for aceclofenac at 275 nm and for ibuprofen at 221 nm. All the dissolution experiments were conducted in triplicate (n=3).

RESULTS AND DISCUSSION

Directly compressible vehicles can be prepared by various methods.[8–10] Co-processing is the one of the most widely explored and commercially utilized method for the preparation of directly compressible vehicles. Co-processing of excipients could lead to the formation of excipients with superior properties compared to the simple physical mixtures of their components. The objective of the present study is to prepare and characterize Starch-PEG co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. Starch-PEG co-processed excipient was prepared by gelatinizing potato starch in the presence of PEG 1500 and drying the resulting mass. The prepared Starch-PEG co-processed excipient was characterized by determining various physical and micromeritic properties. The Starch-PEG co-processed excipient prepared was granular, discrete and free flowing. The physical and micromeritic properties of Starch-PEG co-processed excipient prepared are summarized in Table 1.

The Starch-PEG co-processed excipient prepared was charred at 210^{0}C. It is insoluble in water and aqueous fluids of pH 1.2, 4.5 and 7.4. It exhibited high swelling in water and the swelling index was found to be 445 %. The flow properties of the Starch-PEG co-processed excipient prepared were determined by measuring bulk density, angle of repose and compressibility index. The results given in Table 1 indicated that the excipient prepared has excellent flow properties. As the Starch-PEG co-processed excipient possesses excellent flow properties and swelling character, it is considered as a promising directly compressible vehicle with good disintegration characters for direct compression of tablets.

Table 1: Physical and Micromeritic Properties of Starch-PEG 1500 Co-processed Excipient.

S.No.	Property/Test	Result
1.	Melting point	Charred at 210^0c
2.	Solubility	Insoluble in water and aqueous fluids of acidic and alkaline pHs.
3.	Swelling Index (%)	High Swelling in Water. Swelling Index is 445%
4.	pH (1% aqueous dispersion)	6.5
5.	Particle size (µm)	20/100 mesh
6.	Bulk density (g/cc)	0.833
7.	Tapped density (g/cc)	0.984
8.	Angle of repose (^{o})	16.17
9.	Compressibility index (%)	15.38

Blends of Starch-PEG co-processed excipient and selected drugs (aceclofenac and ibuprofen) also exhibited excellent to good flow properties. The estimated bulk density values of Starch-PEG co-processed excipient would also contribute to its good flow.

To evaluate the Starch-PEG co-processed excipient as directly compressible vehicle (DCV), tablets (i) aceclofenac (50 mg) and (ii) ibuprofen (50 mg) were prepared by direct compression method employing Starch-PEG co-processed excipient as DCV. The tablets were prepared as per the formulae given Table 2. All the tablets prepared were evaluated for content of active ingredient, hardness, friability, and disintegration time and dissolution rate. The results are given in Table 3. Hardness of the tablets was in the range 5.0 - 5.5 Kg/sq.cm. Weight loss in the friability test was in the range 0.87 – 1.12 %.The drug content of the tablets was within 100 ± 3% of the labeled claim. All the tablets formulated disintegrating rapidly within 15 seconds. As such all the tablets prepared employing the Starch-PEG co-processed excipient were of good quality with regard to drug content ,hardness, friability and disintegration time.

Table 2: Formulae of Tablets Prepared By Direct Compression Method Employing Starch - PEG 1500 Co- processed Excipient.

Ingredient (mg/tablet)	Tablet Formulation	
	Aceclofenac	Ibuprofen
API	50	50
Starch-PEG 1500 Co-processed excipient (20/100 mesh)	161	161
PVP K 30	4.6	4.6
Crospovidone	9.2	9.2
Talc	4.6	4.6
Magnesium stearate	4.6	4.6
Tablet weight (mg)	234	234

Table 3: Physical Properties of Various Tablets Prepared By Direct Compression Method Employing Starch-PEG Co-processed Excipient

Formulation	Hardness (kg/sq.cm)	Friability (% weight loss)	Disintegration time (sec)	Drug content (mg/tablet)
Aceclofenac tablets	5.5	1.12	05-10	49.50
Ibuprofen tablets	5.0	0.87	10-15	49.25

Dissolution rate of formulated and commercial tablets was studied in each case. The results of the dissolution rate study are given in Table 4. With both the two drugs, the tablets formulated employing Starch-PEG co processed excipient gave rapid dissolution of the contained drug. Dissolution was very rapid and complete with in 15-20 min in all the cases and fulfilled the official (I.P 2010) dissolution rate test specification prescribed in each case.

Table 4: Dissolution Parameters of Tablets Prepared by Direct Compression Method Employing Starch – PEG Co-processed Excipient and Commercial Tablets.

Formulation	Dissolution Parameter			Official Dissolution Rate Specification	Dissolution Observed
	PD_{10} (%)	DE_{20} (%)	K_1 (min^{-1})		
Aceclofenac Tablets Formulated	88.05	78.90	0.187	NLT 70 % in 45 min in phosphate buffer of pH 6.8 (I.P, 2010)	70 % in 5 min
Aceclofenac Tablets Commercial	81.36	69.96	0.055	NLT 70 % in 45 min in phosphate buffer of pH 6.8 (I.P, 2010)	94 % in 45 min
Ibuprofen Tablets Formulated	81.79	74.30	0.118	NLT 50 % in 30 min in phosphate buffer of pH 7.2 (I.P, 2010)	50 % in 4 min
Ibuprofen Tablets Commercial	98.5	82.83	0.420	NLT 50 % in 30 min in phosphate buffer of pH 7.2 (I.P, 2010)	98.5% in 10 min

Dissolution data were analyzed as per zero order and first order kinetics. Drug dissolution from the tablets followed first order kinetics with correlation coefficient (r) values > 0.985. The corresponding first order release dissolution rates (K_1) are calculated from the slope of the first order linear dissolution plots. The dissolution efficiency (DE_{20}) values were calculated as suggested by Khan.[11] The dissolution parameters are summarized in Table 4. Drug dissolution from the formulated tablets was rapid and higher than that from commercial tablets in the case of aceclofenac. In the case of ibuprofen commercial tablets gave relatively higher dissolution rates than the formulated tablets, but both gave 100 % dissolution in 15 min.

Thus Starch-PEG co-processed excipient could be used as directly compressible vehicle in the formulation development of compressed tablets. Tablets of aceclofenac and ibuprofen formulated employing Starch-PEG co-processed excipient exhibited rapid disintegration and dissolution rate characteristics and fulfilled the official (I.P) specifications with regard to various physical properties and dissolution characteristics.

CONCLUSION

Starch-PEG co-processed excipient prepared was found to be granular, discrete and free flowing. It is insoluble in water and aqueous fluids of pH 1.2, 4.5 and 7.4. It exhibited high swelling (445%) in water. Starch-PEG co-processed excipient has excellent flow properties alone and as blends with selected drugs it exhibited excellent to good flow properties. Tablets of (i) aceclofenac and (ii) ibuprofen prepared by direct compression method employing Starch-PEG co-processed excipient as DCV were of good quality with regard to drug content, hardness, friability and disintegration time. All the tablets formulated employing Starch-PEG co-processed excipient disintegrated rapidly within 15 seconds. With both the two drugs, the tablets prepared gave rapid dissolution of the contained drug. Dissolution was complete with in 15-20 min in all the cases and fulfilled the official (I.P 2010) dissolution rate test specification prescribed in each case. Thus Starch-PEG co-processed excipient developed in this study was found to be a promising directly compressible vehicle for the preparation of compressed tablets with fast dissolution characteristics.

REFERENCES

1. D. Reimerdes: The Near Future of Tablet Excipients. Manufacturing Chemist, 1993; 64(7): 14-15.
2. K. M. Dev et al., Coprocessed Microcrystalline Cellulose and Calcium Carbonate and Its Preparation. US Patent No.4, 744, 987 to FMC Corporation (Philadelphia, PA), 1988.
3. G. K. Bolhius and Z. T .Chowhan: Materials for Direct Compaction. Pharmaceutical Powder Compaction Technology. G.Alderborn and C.Nystron, Eds. Marcel Dekker Inc., New York, NY, 1996; 419-500.
4. K.P.R.Chowdary and Sunil Kumar: Formulation development of selected drugs by direct compression method. IJPRD, 2011; Vol 3(6): 273-279.
5. Martin A: Physical Pharmacy. Lippincott Williams &Wilkins. Baltimore, 2001:423-454.
6. Cooper J, Gunn C: Powder flow and compaction. Tutorial Pharmacy. CBS Publications, New Delhi, India, 1986; 211-233.
7. Aulton ME, Wells TI: Pharmaceutics; The Science of dosage form design. Churchill Livingstone, London, England, Edition, 1988; 2: 89-90.
8. Reimedes, D: The Near Future of Tablet Excipients. Manuf. Chem, 1993; 64: 14-15.
9. Shangraw, R.F., Wallace, J.W., and Bowes, F.M: Morphology and functionality in Tablet Excipients for Direct Compression. Pharm. Technol, 1987; 11: 136-143.10.
10. Bolhuis G.K and Chowhan Z.T: Materials for Direct Compression. Pharmaceutical Powder Compaction Technology. Marcel Dekker, USA, 1996; 7: 419-499.
11. Khan K.A., J. Pharm. Pharmacol, 1975; 27: 48.