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Research Article

PREPARATION, CHARACTERIZATION AND EVALUATION OF PGS-PVP-AEROSIL CO-PROCESSED EXCIPIENT AS DIRECTLY COMPRESSIBLE VEHICLE IN TABLETS FORMULATION

K.V.N.R.Aishwarya *, K.V.Ratnam

Aditya Pharmacy College, AdityaNagar, ADB Road, Surampalem-533437, Andhra Pradesh, India.

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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 pregelatinised starch-polyvinyl pyrrolidone K-30 - Aerosil (PGS-PVP-Aerosil) co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. PGS-PEG-Aerosil co-processed Excipient was prepared by gelatinizing rice starch in the presence of PEG 1500 and Aerosil 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. The new co-processed excipient prepared was crystalline, discrete, fine and free flowing powder. It is insoluble in water and aqueosus buffers of pH 1.2, 4.5 and 7.4 and in several organic solvents. It exhibited high swelling (284%) in water. The new excipient developed (PGS- PVP-Aerosil) exhibited excellent flow properties alone and as blends with selected drugs. Tablets of i) Aceclofenac and ii) Sulphamethoxazole prepared employing PGS-PVP-Aerosil co-processsed excipient alone as directly compressible vehicle were found to be soft and fragile. Blend of PGS-PVP-Aerosil co-processed excipient exhibited good flow characteristics. Tablets of i) Aceclofenac and ii)Sulphamethoxazole prepared by direct compression method employing blend PGS- PVP-Aerosil as directly compressible vehicle was found to be of good quality with regard to drug content, hardness, friability, disintegration time and dissolution rate. All the tablets disintegrated rapidly within 60-80 sec and gave rapid dissolution of the contained drug fulfilling the official dissolution rate test specification prescribed in each case. Thus PGS-PGVP-Aerosil co-processed excipient developed was found to be a promising directly compressible vehicle for the preparation of compressed tablets with fast dissolution characteristics.

INTRODUCTION

Direct compression is the preferred method for the preparation of tablets [1].

***Address for correspondence**

K.V.N.R.Aishwarya*
D/O K.N.V.S.Satyanarayana,
Dno: 44-11- 37,Bose Statue Street,
Annapurnammapeta, Rajahmundry-533101,
East Godavari District,AndhraPradesh.
E-mail: aishupharma09@gmail.com
Phone Number: 9949736626

It offers several advantages[2-3] .Notable among them are (i) It is economical compared to wet granulation since it requires fewer unit operations (ii) More suitable for moisture and heat sensitive APIs since it eliminates wetting and drying steps (iii) Changes in dissolution profile are less likely to occur in tablets made by direct compression method on storage than in those made from granulations[4].This is extremely important because the official compendium now requires dissolution specifications in most solid dosage forms[5]. Disintegration or dissolution is the rate-limiting step in

absorption in the case of tablets of poorly soluble API prepared by wet granulation. The tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with dissolution fluid and exhibits comparatively faster dissolution. The direct compression process is mainly influenced by the properties of the excipients. The physico mechanical properties of excipients that ensure a robust and successful process are good flowability, good compressibility, low or no moisture sensitivity, low lubricant sensitivity, and good machine ability even in high –speed tableting machinery with reduced dwell times [6]. The majority of the excipients that are currently available fail to live up to these functionality requirements, thus creating the opportunity for the development of new high-functionality excipients. 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 [7]. 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[8], 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 (SPVP), which is the most widely used co-processed excipient[9].The major objective of the present study is to prepare and characterize pregelatinized starch-poly vinyl pyrrolidone (PGS-PVP) co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. PGS-PVP co- processed excipeint was prepared by gelatinizing potato starch in the presence of PVP and drying the resulting mass.

Materials &Methods:

Aceclofenac and sulphamethoxazole were gift samples from M/s Natco Pharma Ltd., Potato starch from SDFCL. Mumbai., Poly vinyl Pyrrolidone K-30 from Sigma Chemicals. Mumbai., Lactose, methanol, chloroform,di chloromethane from Qualigens., Talc, magnesium stearate were procured from LOBA CHEME Mumbai., All other materials used were of Pharmacopoeial grade.

Methods:

Preparation of PGS-PVP-Aerosil Coprocessed Excipient:

Potato starch (49 parts) and PVP K-30 (1 part) and Aerosil (0.4 parts) were dispersed in 20 parts of water to form smooth slurry. Purified water (40 parts) was taken in a separate beaker and heated to boiling. Starch-PVP-Aerosil slurry was added to boiling water while stirring. Stirring and heating was continued for 15 to 20 minutes to form a thick mass. To the massformed, acetone (40 parts) was added and mixed thoroughly to remove the water in the product formed. The product formed was collected by filtration and further dried at 80^0C until dry. The dried product was grinded and sized to obtain -72+100 mesh sized particles.

Characterization of New Co-Processed Excipient Prepared:

The new co-processed excipient prepared was evaluated for the following:

Solubility: Solubility of PGS-PVP-Aerosil coprocessed excipient was tested in water, aqueous buffers of pH 1.2, 4.5, and 7.4 and organic solvents such as alcohol, dichloromethane, chloroform, acetone and petroleum ether.

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

Melting Point: Melting point was determined by using melting point apparatus (Digimelt).

Swelling Index [10]***:*** The new excipient prepared(500 mg) was added to 10 ml of water and light liquid paraffin taken in two different graduated test tubes and mixed. The dispersions in the tubes were allowed to stand for 24 h. The volume of the sediment in the tubes was recorded. The swelling index of the material was calculated as follows.

Moisture Absorption: The hygroscopic nature of the new excipient prepared was evaluated by moisture absorption studies in a closed desiccator at 84% relative humidity and room temperature.

Particle Size: Particle size analysis was done by sieving using standard sieves.

Bulk Density [11]***:*** Bulk density (g/cc) was determined by three-tap method in a graduated cylinder.

Angle of Repose [12]**:** Angle of repose was measured by fixed funnel method.

Compressibility Index [13]**:** Compressibility index (CI) was determined by measuring the initial volume (V_0) and final volume (V) after hundred tapings of a sample of the product in a measuring cylinder. CI was calculated using the equation

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

***Estimation of Aceclofenac*:**

An UV spectrophotometric method based on the measurement of absorbance at 274 nm in phosphate buffer of pH 7.4 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 1.76 % and 0.18 % respectively. No interference by excipients used in the study was observed.

***Estimation of Sulphamethoxazole*:**

An UV spectrophotometric method based on the measurement of absorbance at 276 nm in 0.1 N Hcl was used for the estimation of Sulphamethoxazole. 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 1.87 % and 0.45 % respectively. No interference by excipients used in the study was observed.

***Preparation of Tablets by Direct Compression Method*:**

Tablets of (i) Aceclofenac (100 mg) and (ii) Sulphamethoxazole (100 mg) were prepared by direct compression method as per the formulae given in the Table 2 employing PGS-PVP-Aerosil 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 directly compressed into tablets on a 10-station tablet punching machine (Rimek) to a hardness of 3-4 kg/cm2 using 12 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 single unit disintegration test apparatus (Make paramount) using water as a test fluid.

Estimation of Drug Content in the Tablets[14]:

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 upto 100 ml with methanol. The solution was then suitably diluted with phosphate buffer 7.4 in case of aceclofenac and with 0.1 N HCl of in the case of sulphamethoxazole. The absorbance of the solutions was measured at 276 nm and 274 nm respectively in the case of aceclofenac and sulphamethoxazole . Drug content of the tablets was calculated using the standard calibration curve in each case.

Dissolution Rate study [15]**:**

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 7.4 (900ml), and 0.1N HCl (900ml) were used as dissolution fluids for aceclofenac and sulphamethoxazole respectively. One tablet was used in each test. At a temperature, 37 ± 10^0C was maintained throughout. Samples of dissolution medium (5ml) were withdrawn through a filter (0.45 µ) at different time intervals and assayed for for aceclofenac at 276 nm and at 274 nm for sulphamethoxazole. All the dissolution experiments were conducted in triplicate (n=3).

RESULTS AND DISCUSSION

Directly compressible vehicles can be prepared by various methods [1-3]. 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 pregelatinized starch-poly vinyl pyrrolidone (PGS-PVP) co-processed excipient and to evaluate its application as directly compressible vehicle in tablet formulations. PGS-PVP co-processed excipient was prepared by gelatinizing potato starch (49 parts) in the presence of PVP (1 part).The prepared PGS-PVP co-processed excipient was characterised by

determining various physical and micromeritic properties[16]. The PGS-PVP co-processed excipient prepared was found to be crystalline, discrete and free flowing powder. It could be ground to various particle sizes by grinding in a dry mortar. Particles of size -72+100 mesh (179.5 μm) were collected and used for further studies. The physical and micromeritic properties of PGS-PVP co-processed excipient prepared are summarized in Table – 1. The PGS-PVP co-processed excipient prepared was charred at 250^0C.It is insoluble in water and aqueous fluids of pH 1.2, 4.5 and 7.4 and also in several organic solvents such as alcohol, methanol, dichloromethane, acetone, chloroform and petroleum ether. It exhibited high swelling in water and the swelling index was found to be 284 %.

The flow properties of the PGS-PVP co-processed excipient preparеprepared were determined by measuring bulk density, angle of repose and compressibility index. The results given in Table 4 indicated that the excipient prepared has excellent flow properties. Directly compressible vehicles should be free flowing.Flowability is required in order ensure homogeneous and rapid flow of powder for uniform die filling. During the short dwell-time (milliseconds), the required amount of powder blend should be transferred into die cavities with reproducibility of ± 5%. As the PGS-PVP co-processed excipient possesses excellent flow properties, it is considered as a promising directly compressible vehicle for direct compression of tablets. Blends of PGS-PVP co-processed excipient and selected drugs (sulphamethoxazole, paracetamol and aceclofenac) also exhibited excellent to good flow properties. The estimated bulk density values of PGS-PVP co-processed excipient would also contribute to its good flow.

Evaluation of PGS-PVP co-processed excipient as directly compressible vehicle:

To evaluate the PGS-PVP co-processed excipient as directly compressible vehicle (DCV), tablets of (i) sulphamethoxazole (ii) paracetamol and (iii) aceclofenac were prepared by direct compression method employing PGS-PVP co-processed excipient as DCV at strength of 60% in the formula. The tablets were prepared as per the formulae given Table 5. 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 6. Hardness of the tablets was in the range 4.0 - 5.0 Kg/sq.cm. Weight loss in the friability test was in the range 1.45 – 2.10%.The drug content of the tablets was within 100 ± 3% of the labelled claim. All the tablets formulated disintegrating rapidly within 3.5 min. As such all the tablets prepared employing the PGS-PVP co-processed excipient were of good quality with regard to drug content ,hardness, friability and disintegration time. .With all the three drugs,the tablets prepared gave rapid dissolution of the contained drug. The dissolution was complete (100 %) within 20 min and fulfilled the official (IP/USP) dissolution rate test specification prescribed in each case. The dissolution parameters are summarized in table – 4.

CONCLUSIONS:

1. The new co-processed excipient prepared was crystalline, discrete, fine and free flowing powder.
2. It is insoluble in water and aqueous buffers of pH 1.2, 4.5 and 7.4 and in several organic solvents.
3. It exhibited high swelling (284%) in water.
4. The new excipient developed (PGS- PVP-Aerosil) exhibited excellent flow properties with selected drugs.
5. Tablets of i) Aceclofenac and ii) Sulphamethoxazole prepared employing PGS-PVP-Aerosil coprocesssed excipient alone as directly compressible vehicle were found to be soft and fragile.
6. Blends of PGS-PVP-Aerosil co-processed co-processed excipient exhibited good flow characteristics.
7. Tablets of i) Aceclofenac and ii)Sulphamethoxazole prepared by direct compression method employing PGS-PVP-Aerosil coprocessed excipient as directly compressible vehicle were found to be of good quality with regard to drug content, hardness, friability, disintegration time and dissolution rate.
8. All the tablets disintegrated rapidly within 60-80 sec and gave rapid dissolution of the contained drug fulfilling the official dissolution rate test specification prescribed in each case. Thus, PGS-PEG-Aerosil co-processed excipient developed was found to be a promising directly compressible vehicle for the preparation of compressed tablets with fast dissolution characteristics.

Table 1: Physical and Micromeritic Properties of PGS-PVP-Aerosil Co-processed Excipient

S.No.	Property/Test	Result
1.	Melting point	Charred at 250^0c
2.	Solubility	Insoluble in water, methanol, alcohol, acetone, chloroform, dichloromethane and petroleum ether
3.	Swelling Index (%)	High swelling in water Swelling index 284%
4.	pH (1% aqueous dispersion)	6.8
5.	Particle size (μm)	72/100 mesh (287 μm)
6.	Bulk density (g/cc)	0.436
7.	Tapped density (g/cc)	0.464
8.	Angle of repose (^{o})	25.17
9.	Compressibility index (%)	7.8

Table 2: Formulae of Tablets Prepared By Direct Compression Method Employing PGS – PVP – Aerosil Co-processed Excipient

Ingredient (mg/tablet)	Tablet Formulation	
	Sulphamethoxazole	Aceclofenac
Sulphamethoxazole	100	-
Aceclofenac	-	100
PGS-PVP Co-processed excipient (72/100 mesh)	264	264
Lactose	58.4	58.4
Talc	8.8	8.8
Magnesium stearate	8.8	8.8
Tablet weight (mg)	440	440

Table 3: Physical Properties of Various Tablets Prepared by Direct Compression Method Employing PGS –PVP-Aerosil Co-processed Excipient

Formulation	Hardness (kg/sq.cm)	Friability (% weight loss)	Disintegration time(min-sec)	Drug content (mg/tablet)
Aceclofenac tablets	4.0	0.72	1-20	98.5
Sulphamethoxazole tablets	4.5	0.93	1-00	101.6

Table 4: Dissolution Parameters of Tablets Prepared by Direct Compression Method Employing PGS-PVP-Aerosil Co-processed Excipient

Tablet Formulation	DE_{30} (%)	$K_1 \times 10^2$ (min^{-1})	PD_{10} (%)	T_{50} (min)
Aceclofenac tablets	55.45	0.046	55.62	10
Sulphamethoxazole tablets	72.74	0.069	100	9

Fig 1: Zero order plot for Aceclofenac and Sulphamethoxazole tablets Employing PGS-PVP-Aerosil Co-processed Excipient

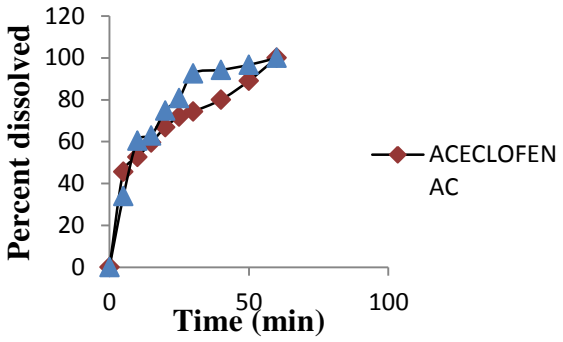
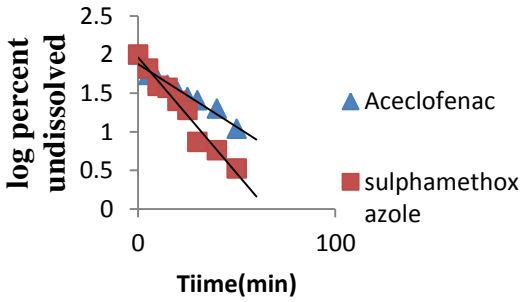


Fig 2: First order plot for Aceclofenac and Sulphamethoxazole tablets Employing PGS-PVP-Aerosil Co-processed Excipient



REFERENCES:

1. Shangraw RF, Direct Compression Tableting, Encyclopedia of Pharmaceutical Technology.Vol(4), 2nd ed.Newyork: Marcel Dekker, USA, 1988,pp.85-160.
2. Armstrong NA, Selection of excipients for direct compression tablet formulation. Pharm.Technol.Eur.1989; 24-30.
3. JivrajM,Martini LG, Thomson CM, An Overview of the Different Excipients Useful for the Direct Compression of Tablets, PSTT.2000;3:58-63.
4. Rubinstein MH, Tablets Pharmaceutics: The Science of Dosage of Form, Churchill, UK, Isted, 1998, pp.304-321.
5. Banker UV, Role of Ingredients and Excipients in Developing Pharmaceuticals., Manuf. Chem.1994;65:32-34.
6. N.A.Armstrong and L.P.Palfrey, The Effect of Machine Speed on the Consolidation of Four Directly Compressible Tablet Diluents ,J.Pharm. Pharmacol.41, 149-151(1989).
7. D.Reimerdes, The Near Future of Tablet Excipients ,Manufacturing Chemist, 64(7),14-15(1993)
8. 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.
9. G.K.Bolhius and Z.T.Chowhan, Materials for Direct Compaction. In Pharmaceutical Powder Compaction Technology, G.Alderborn and C.Nystron, Eds.(Marcel Dekker Inc., New York, NY, 1996), pp.419-500.
10. K.P.R.Chowdary and Sunil Kumar: Formulation development of selected drugs by direct compression method. IJPRD, 2011; Vol 3(6): 273-279.
11. Martin A: Physical Pharmacy. Lippincott Williams &Wilkins. Baltimore, 2001:423-454.
12. Cooper J, Gunn C: Powder flow and compaction. Tutorial Pharmacy. CBS Publications, New Delhi, India, 1986: 211-233.
13. Aulton ME, Wells TI: Pharmaceutics; The science of dosage form design. Churchill Livingstone, London, England, Edition 2, 1988: 89-90.
14. Jivraj M, Martini LG, Thomson CM, an Overview of the Different Excipients Useful for the Direct Compression of Tablets, PSTT.2000; 3:58-63.
15. Rubinstein MH, Tablets Pharmaceutics: The Science of Dosage of Form, Churchill, UK, Isted, 1998, pp.304-321.