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(Research Article)

Development of Fast Disintegrating Tablet of Celecoxib

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ABSTRACT

The demand for orally disintegrating tablets has been growing during the last decade especially for the geriatric and pediatric patients. Celecoxib is a sulpha non-steroidal anti-inflammatory drug (NSAID) and selective COX-2 inhibitor administered orally as analgesic and anti-inflammatory drug in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation and menstrual symptoms, and to reduce numbers of colon and rectum polyps in patients with familial adenomatous polyposis. The poor aqueous solubility of the drug leads to variable dissolution rates. The present work has been an attempt to prepare oro-dispersible tablets of celecoxib with a combination of superdisintegrants, amino acids, and sweeteners. Camphor was used as a sublimating agent. Tablets are prepared by direct compression and mannitol is used as bulking agent. The tablets were evaluated for weight variation, hardness, thickness, friability, disintegrating time, and drug release.

Key Words: Fast dissolving tablet, Celecoxib, Orodispersible tablet, Solid dispersion.

INTRODUCTION

Of the various orally administered dosage forms, the tablet is one of the most preferred. In recent years, the task of developing rapidly disintegrating tablets has been accomplished by using suitable diluents and superdisintegrants. Thus it is rapidly gaining acceptance due to better patient compliance, improving performance and exclusive market. Celecoxib is sulpha NSAID, acting by inhibition of prostaglandins and selective, noncompetitive COX-2 enzyme inhibitor used as analgesic, anti-inflammatory in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, and painful menstruation. Celecoxib is preferred over conventional NSAIDs, as the latter may lead to serious gastrointestinal complications such as ulcer, severe bleeding and perforation, resulting in hospitalization and even death. Celecoxib is practically insoluble in water (0.003 mg/mL). Techniques that have been used to improve solubility, dissolution and consequently bioavailability of poorly water-soluble drugs include micronization, use of surfactants, and the formation of solid dispersions. Among the various hydrophilic carriers used in the formation of solid dispersions, polyvinyl pyrrolidone is most commonly used.

The aim of the present study was to evaluate the physicochemical properties of solid dispersions of celecoxib-PVP-K30 and to prepare oro-dispersible tablets of celecoxib having enhanced dissolution rate with the aid of superdisintegrant like Crospovidone.

MATERIALS AND METHODS

Materials

Celecoxib, Polyvinylpyrrolidone, Mannitol (granular), Crospovidone, Colloidal silicon dioxide, Methanol, Orange flavor, talk and Magnesium stearate were purchased from S. K. Enterprises, Pune. All other chemicals and reagents used were of pharmaceutical grade.

Preparation of Solid Dispersions of Celecoxib with PVP-K 30

Accurately weighed quantities of physical mixtures of celecoxib and PVP-K30 in proportions of 1:1, 1:2, 1:3, and 1:4were triturated in a glass mortar with a small volume of methanol. The thick slurry was kneaded for 45 min and then dried at 50^0C to constant weight. The dried mass was pulverized and sifted through sieve #100 and stored in a desiccator.

Evaluation of Solid Dispersions

All four batches of solid dispersion were evaluated for their drug content and dissolution profile to select the optimized batch.

Drug content analysis

Drug content was determined by dissolving the 100 mg powdered samples of solid dispersion equivalent to 100 mg of celecoxib into 100 ml distilled water containing 1% SLS. Allow to stand the samples overnight. Then filter the

solution and samples were assayed for celecoxib content by measuring the absorbance on UV-spectrophotometer at 254 nm. The experiment was conducted in triplicate. The method obeyed Beer's law in the concentration range of 0-10 µg/ml.

In-vitro dissolution study

Dissolution study of celecoxib as such and it's solid dispersions were performed using USP Apparatus 2 with a paddle stirrer (Electrolab, Mumbai, India) in a 900 ml distilled water containing 1% SLS at 37 °C with a rotation speed of 50 rpm to maintain sink condition. Powdered samples of each preparation equivalent to 100 mg of celecoxib were added to the dissolution medium. At appropriate time intervals, 5 mL of the mixture was withdrawn through a filter (0.45µ). The initial volume was maintained by adding 5 mL of fresh dissolution medium. The samples were assayed for celecoxib content by UV spectrophotometry at 254 nm.

Formulation of Tablets of Celecoxib- PVP K-30 Solid Dispersion

The tablet formulations C-1 to C-9 were developed from Celecoxib-PVP-K30 solid dispersion (1:2) that has shown maximum in-vitro dissolution. The raw materials were passed through a 60-mesh screen before mixing. A powdered 1:2 solid dispersion containing an amount of Celecoxib equivalent to 75 mg was mixed with the other excipients (Table 1) and evaluated for bulk characterization. The blend was directly compressed on a RIMEK rotary tablet machine using 12-mm diameter, flat-face round punches (Jaguar General Machines Pvt. Ltd, Mumbai). The tablet weight was adjusted to approximately 400 mg. After that the compressed tablets were dried for 6 hours for the sublimation of camphor. The tablets were stored in a tightly closed glass container and evaluated for various quality control tests in triplicate.

Evaluation of the Prepared Tablets

Tablet crushing strength and friability were determined using a Monsanto Hardness tester and a friability test apparatus (Lab India FT-1012), respectively. The disintegration times were measured using a modified disintegration method. The tablet was carefully put in the centre of the petri dish (10cm diameter, filled with 10 mL of water), and the time for the tablet to disintegrate completely into fine particles was noted. For drug content analysis, 20 tablets were accurately weighed and finally powdered. The quantity of powder equivalent to 100mg of Celecoxib was taken into a 100 ml volumetric flask, and dissolved in 25 ml of methanol and volume adjusted to 100 ml with methanol and filtered. Filtrate was diluted suitably and assayed for drug content at 254 nm using UV spectrophotometer.

In-vitro dissolution study of the tablets was conducted using USP dissolution apparatus-1, at 50 rpm using water containing 1.0 %w/v SLS as a dissolution media at $37^{o}C \pm 0.5^{o}C$. Samples were withdrawn at various time intervals. Filtered through a 0.45 micron membrane filter, diluted, and assayed at 254nm using UV spectrophotometer.

RESULTS AND DISCUSSION

Evaluation of Solid Dispersions

Drug content analysis

All the solid dispersions (SDS) were found to be low values of content variation (<1.0%) in percent drug content indicated uniformity of drug content in each batch of solid dispersions.

Dissolution Studies

Dissolution rate of pure celecoxib as such and it's all prepared solid dispersions were carried out and drug release values at 20 and 60 min are shown in Table 2. The onset of dissolution of pure celecoxib was very low (21.04 % in 1 hr.), signifying a strong necessity to improve the dissolution of celecoxib.The presence of PVP-K30 increases the dissolution rate of celecoxib up to a drug-to-polymer ratio of 1:2. Due to the formation of a viscous boundary layer around the drug particles, leading to a decrease in the dissolution rate at higher ratios.

Evaluation of Celecoxib Fast-Dissolving Tablets

Wicking and capillary action are major factors in the ability of superdisintegrants to function. All the prepared tablets were characterized by weight variation, hardness, thickness and found within the pharmacopoeia limits. As a result, the tablet containing optimum concentration of crosspovidone and camphor showed the shortest time for disintegration because the major mechanism of disintegration for crosspovidone is capillary action with good strength (0.42% friability), shortest disintegration time (Table 5). Batch C-5 is optimized batch, which shows improved dissolution compared to all other batches.

CONCLUSION

The present study conclusively indicates that the tablets prepared from solid dispersion of Celecoxib: PVP (K-30) in the ratio of 1:2 and containing 4% Crosspovidone and Camphor 4% as sublimating agent. Batch C-5 shows promising improvement in the dissolution characteristics of Celecoxib and hence may improve its bioavailability.

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Table 1: Formulation of Celecoxib Fast Dissolving Tablets

Tablet ingredients (mg) /Formulation code	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
Celecoxib:PVP K-30 (1:2)	225	225	225	225	225	225	225	225	225
Glycine	20	20	20	20	20	20	20	20	20
Mannitol (granular)	125	121	117	121	117	113	117	113	109
Crospovidone	12	12	12	16	16	16	20	20	20
Camphor	12	16	20	12	16	20	12	16	20
Orange flavour	3	3	3	3	3	3	3	3	3
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight (mg)	400	400	400	400	400	400	400	400	400

Table 2: Dissolution studies of Pure Celecoxib and Solid Dispersions

Drug Release at time	20 min	60 min
Celecoxib	5.64 ± 0.5	21.04 ± 0.6
Drug/PVP-K30 SD (1:1)	18.62 ± 0.3	54.26 ± 4.4
Drug/PVP-K30 SD (1:2)	31.27 ± 1.8	81.45 ± 2.7
Drug/PVP-K30 SD (1:3)	28.34 ± 1.1	69.31 ± 2.6
Drug/PVP-K30 SD (1:4)	26.58 ± 0.9	64.42 ± 1.3

Table 3: Bulk Characterization of Powder Blends of a Drug and Excipients

Characterization of powder blends/ Formulation code*	Angle of Repose	Bulk Density (g/cm^3)	Tapped density (g/cm^3)	Compressibility index (%)	Flow Ability
C-1	25.12	0.571	0.669	14.54	Excellent
C-2	26.35	0.586	0.684	14.32	Excellent
C-3	27.21	0.579	0.674	14.09	Excellent
C-4	26.65	0.568	0.667	14.35	Excellent
C-5	25.95	0.578	0.678	14.17	Excellent
C-6	24.84	0.588	0.688	14.03	Excellent
C-7	25.74	0.546	0.650	14.18	Excellent
C-8	24.48	0.521	0.6528	14.06	Excellent
C-9	24.16	0.571	0.673	13.91	Excellent

Table 4: Evaluation of Celecoxib Fast-Dissolving Tablets

Tablet ingredients(mg)/ Formulation code	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
Friability (%)	0.49	0.56	0.64	0.65	0.60	0.91	1.02	1.16	1.37
In vitro DT (sec)	36-40	33-36	32-36	30-34	27-30	31-35	31-36	36-39	38-42
Q_{30} (mins)	81.95	82.23	83.43	83.82	85.95	87.65	88.95	90.65	90.95

Table 5: Percentage cumulative drug released data of formulations (mean±sd) (n=3)

Time (min)	Drug	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
0	0	0	0	0	0	0	0	0	0	0
5	1.26	21.95	22.56	22.52	23.97	25.27	24.95	26.16	26.79	27.06
10	2.19	41.69	42.39	44.01	43.34	46.33	45.69	46.27	47.19	48.25
20	5.64	69.83	71.04	72.24	73.05	75.98	74.52	76.69	78.25	79.41
30	14.51	81.95	82.23	83.43	83.82	85.95	87.65	88.95	90.65	90.95
60	21.04	91.14	92.74	93.59	94.16	95.76	96.24	96.64	97.11	98.48

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