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Original Article

Development, evaluation and characterization of surface solid dispersion for solubility and dispersion enhancement of irbesartan

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ABSTRACT

Aim: The present study is to prepare and assess Irbesartan loaded surface solid dispersions (SSD) for enhancing the solubility and bioavailability of poor soluble drug.
Method: Irbesartan loaded SSD were prepared by co-evaporation method by using five different super disintegrants like crospovidone, croscarmellose sodium, potato starch, sodium starch glycolate and microcrystalline cellulose in three different drug–carrier ratios and evaluate for the in vitro drug release.
Results: The prepared formulations were white in colour and free flowing. The spectral data reveals that there are no drug-polymer interactions. The P-XRD studies showed decrease in crystallinity of drug formulations when compared to the pure state of the drug. The SEM study was found to be irregular matrices due to the porous nature of the carrier with the fine particles of the drug embedded in it. The in vitro dissolution studies of surface solid dispersion of crospovidone with drug to carrier ratio of 1:10 showed highest dissolution rate with the dissolution efficiency of 98.18% (10 min) in comparison to the other formulations due to deposition of drug on the surface of an inert carrier leading to a reduction in the particle size of the drug, thereby providing a faster dissolution rate.
Conclusion: The surface solid dispersion technique has been shown as a popular approach to improve the dissolution rate of poor soluble Irbesartan.

1. Introduction

Irbesartan (IBS) is 2-butyl-3-[[2-(1H-tetrazole-5-yl)(1,1-biphenyl)-4-yl]methyl]-1,3-diazaspiro[4,4]non-1-en-4-one. IBS displaces angiotensin II from the angiotensin I receptor and produces the blood pressure-lowering effect by antagonizing angiotensin II. It is potentially safe and more tolerable than other classes of antihypertensive drugs. Irbesartan reduces the chances of cardiac failure, sudden death, and death from progressive systolic failure.[1] It belongs to class II drug according to biopharmaceutical classification system (BCS) i.e., low solubility and high permeability. IBS is practically insoluble in water (0.00884 mg/

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mL) and has a high hydrophobicity, with 60–80% oral bioavailability. But theoretically IBS exhibits solubility limited bioavailability and it would be advantageous to increase the solubility of such molecules. Solubility of IBS was found to increases after complexation with polymer like β-CD,[2] wet granulation method,[3] crystal engineering technique,[4] self nanoemulsifying,[5] liquisolid compact technique,[6] solid dispersions technique,[7] spray drying method,[8] fusion and co-solvent techniques[9] and solvent evaporation method.[10]

Preparation of SSD's technique provides deposition of drug on the surface of an inert carrier which leads to a reduction in the particle size of the drug, thereby providing a faster dissolution. Various hydrophilic materials with high surface area can be utilized for deposition of the drug on their surfaces. Surface solid dispersion had been established as a successful method to improve the dissolution rate and the solubility of poor soluble drugs. In the present study, the surface solid dispersion technique was applied in order to improve the dissolution rate of Irbesartan. The carriers used were microcrystalline cellulose, crospovidone, croscarmellose sodium, sodium starch glycolate, microcrystalline cellulose and potato starch. The samples were prepared at various drug-to-carrier weight ratios by co-evaporation method. The prepared SSDs were characterized by using FTIR, DSC, P-XRD, SEM and in vitro dissolution.

2. Materials and methods

2.1. Materials

Irbesartan (IBS) was obtained as a gift sample from Dr. Reddy's Laboratories Ltd. (Hyderabad, India). The super disintegrants (SD) crospovidone (CP), sodium starch glycolate (SSG), potato starch (PS), croscarmellose (CC), microcrystalline cellulose (MC) and solvents used were obtained from S D Fine Chem. Ltd.

2.2. Preparation of surface solid dispersions

The SSD of IBS and SD were prepared by solvent co-evaporation method. The required amount of IBS was dissolved in sufficient amount of methanol. The SD was dispersed in the IBS solution. The different ratios of drug and SD were shown in Table 1. The mixtures were sonicated for 15 min to ensure the intimate mixing. The solvent was then removed, using rotary vacuum evaporator at 50 °C. The residue obtained was dried at 50 °C overnight. The dried mass was pulverized and passed through 80/170 mesh sieves. The products were kept in desiccators for further study.

Table 1 – Formulation and dissolution parameters of irbesartan-Surface solid dispersion (IBS-SSDs) containing different drug (IBS) and super disintegrants (SDs).

S. no	Formulations	IBS: SDs ratio	IBS (mg)	SDs (mg)	%IBS content	MDT	% Dissolution efficacy
1	F01-CP (SSD)	1:1	75	75	93.38	6.002	60.09
2	F02-CP (SSD)	1:5	75	375	94.42	4.768	70.48
3	F03-CP (SSD)	1:10	75	750	97.30	2.316	76.36
4	F04-CP (PM)	1:1	200	200	92.28	7.314	52.32
5	F05-CP (PM)	1:5	100	500	94.31	8.199	66.25
6	F06-CP (PM)	1:10	75	750	95.88	4.219	69.57
7	F07-SSG (SSD)	1:1	75	75	92.28	7.506	62.34
8	F08-SSG (SSD)	1:5	75	375	94.12	5.569	68.59
9	F09-SSG (SSD)	1:10	75	750	96.91	4.146	71.92
10	F10-SSG (PM)	1:1	200	200	92.43	8.039	52.03
11	F11-SSG (PM)	1:5	100	500	94.23	6.549	65.31
12	F12-SSG (PM)	1:10	75	750	95.04	5.103	68.21
13	F13-MC (SSD)	1:1	75	75	92.00	7.763	59.39
14	F14-MC (SSD)	1:5	75	375	93.79	6.378	67.73
15	F15-MC (SSD)	1:10	75	750	95.87	4.791	71.10
16	F16-MC (PM)	1:1	200	200	91.49	8.112	62.97
17	F17-MC (PM)	1:5	100	500	93.17	7.139	65.86
18	F18-MC (PM)	1:10	75	750	94.23	5.457	68.32
19	F19-CC (SSD)	1:1	75	75	92.13	8.434	62.96
20	F20-CC (SSD)	1:5	75	375	93.64	6.804	66.35
21	F21-CC (SSD)	1:10	75	750	95.98	4.887	70.31
22	F22-CC (PM)	1:1	75	75	91.89	8.535	62.47
23	F23-CC (PM)	1:5	75	375	92.13	7.803	64.86
24	F24-CC (PM)	1:10	75	750	93.49	6.027	67.23
25	F25-PS (SSD)	1:1	75	75	91.58	9.334	61.49
26	F25-PS (SSD)	1:5	100	500	93.14	7.704	65.76
27	F25-PS (SSD)	1:10	75	750	95.04	4.987	69.89
28	F25-PS (PM)	1:1	200	200	91.13	9.435	61.06
29	F25-PS (PM)	1:5	100	500	93.09	8.703	64.26
30	F25-PS (PM)	1:10	75	750	93.79	7.027	67.59
31	Market sample	–	75	–	98.68	8.28	69.45
32	Pure IBS	–	75	–	98.21	8.375	58.31