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Research Article

Agglomeration of Antihypertensive Drug by Spherical Crystallization Method

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Abstract:

Hypertension is a key adaptable cardiovascular risk factor. There are several types of drugs that can be used in the management of hypertension. But the perfect treatment strategy remains uncertain for such a common and treatable disease. Various approaches applied for solubility and bioavailability improvement of poorly water-soluble drugs solid dispersion is one of the most successful method for increasing the drug dissolution rate of the drug. Although these techniques have commonly been used to increase dissolution rate of the drug, there are practical limitations with these techniques, the desired bioavailability enhancement may not always be achieved. In the current work, it was concentrated on improvement of the solubility of candesartan drug by spherical crystallization method. Findings were concluded that spherical agglomerates of candesartan prepared using spherical crystallization technique, showed significant improvement in flowability, compatibility, solubility and dissolution rate of the candesartan compared with pure candesartan.

Keywords: Hypertension, Candesartan, Spherical

Introduction:

Hypertension is a major modifiable cardiovascular risk factor. It is well established that a sustained reduction in blood pressure by drugs reduces the incidence of cardiovascular morbidity and mortality. There are several types of drugs that can be used in the management of hypertension. But, the ideal treatment strategy remains uncertain for such a common and treatable disease. In recent years, studies and new guidelines were published addressing management of hypertension. [1] Despite new guidelines, awareness, treatment and control of hypertension are very poor. The most challenging task for research scientist is to formulate a successful drug product of a poorly soluble drug. This occurs mainly because of poor bioavailability. Improving oral bioavailability of the drugs which are given as solid dosage forms remains a challenge for the formulation scientists due to solubility problems. [2] Limited drug absorption resulting in poor bioavailability is paramount amongst the potential problems that can be encountered when delivering an active agent via the oral route. Poorly water-soluble drugs often show poor bioavailability because of low and erratic levels of absorption. The rate limiting process for absorption of poorly soluble drugs from the solid dosage form could be a slow dissolution rate. Various factors affecting the drug absorption from gastrointestinal tract are poor aqueous solubility or poor membrane permeability. Therefore, slow dissolution rate can be overcome by adopting various solubility enhancement techniques such as such as use of surfactants, complexation, polymorphism, salt formation, size reduction and emulsification. Among various approaches applied for solubility and bioavailability enhancement of poorly water soluble drugs solid dispersion is one of the most successful method for increasing the drug dissolution rate of the drug. [3] Although these techniques have commonly been used to increase dissolution rate of the drug, there are practical limitations with these techniques, the desired bioavailability enhancement may not always be achieved. In the current work, it

was concentrated on improvement of the solubility of candesartan drug by spherical crystallization method.

Material and Methods

Identification and collection of all proposed drug material

The drug candesartan and other required excipients were collected from pharma company, Chandigarh as gift sample. All the collected material was used in the for the proposed work.

Organoleptic Characteristics of Candesartan

Organoleptic properties of candesartan were determined by various standard methods. The colour, odour, and taste of the drug were characterized and recorded using descriptive terminology. [4]

Solubility Studies

500 mg of candesartan was weighed and transferred into different conical flask. 50 ml of different dissolution media were transferred into individual conical flask and were closed appropriately. All the flasks were sonicated for 1 hr and the samples were filtered by using 0.45 µ PTFE filter. The clear solution obtained by filtration was suitably diluted with appropriate dissolution media and the absorbance values were noted at 280 nm. Solubility of candesartan in different dissolution media were determined and results were recorded. [5]

Preparation of candesartan spherical agglomerates using spherical crystallization method

Three different organic solvents as good solvent including methyl acetate (MA), ethyl acetate (EA) and isopropyl acetate (IPA) were employed as a dispersed phase for making oil-in-water emulsions (O/W). Crystallization was carried out in a cylindrical vessel equipped with three baffles. Candesartan was dissolved in 15 ml of good solvent. The solvent solutions were then poured dropwise during 3 min, under stirring (500 rpm), into 485 ml of water containing 0.1% w/v emulsifier. Tween 80, SLS, PVP or HPMC were used as emulsifiers. After 15 min agitation by a propeller type stirrer, the agglomerates were separated from the solution by filtration under vacuum and then were placed in a thin layer in an oven at 60°C for 3 h. The solubility of organic solvents in water was the basis of the selection of the solvents in making solvent-in-water emulsion. [6]

Results and Discussion

Organoleptic Characteristics of Candesartan

The drug candesartan was evaluated organoleptic by sensory organs. The color of drug was found white to off-white powder, crystalline in nature with bitter taste and odorless. The findings were recorded in table 5.1

Table 1: Organoleptic Characteristics of Candesartan

Properties	Results
Color	White to off-white Powder
Odor	Odorless
Taste	Bitter
Microscopic examination	Crystalline

Solubility Studies of Candesartan in Different Dissolution Media

Different dissolution media such as 0.1 N Hydrochloric acid, Glycine buffer pH 3.0, Acetate buffer pH 4.5, Phosphate buffer pH 6.8, Phosphate buffer pH 7.2 and pH 2.5 buffer The findings were recorded in table 2.

Table 2: Solubility of drug in water containing stabilizer

S.N.	Dissolution Media	Amount of Drug Soluble(mg/ml)
1	Purified water	0.28
2	0.1 N Hydrochloride	0.22
3	0.1% Polysorbate	0.57
4	pH 3.0 Glycine buffer	0.10
5	pH 4.5 acetate buffer	0.18

Table 3: Formula for candesartan spherical agglomerates

Formulation Code	Candesartan (mg)	SLS (%)	PVP (%)	Tween 80 (%)	HPMC (%)	Methyl acetate (ml)	Ethyl acetate (ml)	Isopropyl acetate (ml)
Can F1	500	0.0250	.....	.....	.....	20	70	10
Can F2	500	0.0500	.....	.....	.....	20	70	10
Can F3	500	.....	0.0250	.....	.....	20	70	10
Can F4	500	.....	0.0500	.....	.....	20	70	10
Can F5	500	.....	.....	0.0250	.....	20	70	10

Conclusion

Finally, it was concluded that spherical agglomerates of candesartan prepared with and without the polymers using spherical crystallization technique, showed significant improvement in flowabilty, compatibility, solubility and dissolution rate of the candesartan compared with pure candesartan. Inclusion of polymers in the spherical agglomeration yields superior results, which in turn depends on type and concentration of polymer. Agglomerates containing Can F5 was considered optimum as it showed bends development in solubility and dissolution rate respectively, compared with pure drug.

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