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Research Article

Impact Of Antisolvent Crystallization On Rate Of Dissolution Of Nifedipine

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ABSTRACT

Aim of the present study was to study the effect of the antisolvent method of crystallization/precipitation on the rate of dissolution using different antisolvent for nifedipine. Recrystallization of the drug was done in DMF, DMSO and ethanol using water as antisolvent. Drug Excipient Compatibility Study was confirmed by FTIR method. Differential scanning calorimetry (DSC) of pure drug and it's solvates were done to confirm the crystalline structure of the and molecular symmetry was assured by XRD studies. Impact of the size of drug and it's solvates n dissolution was confirmed by SEM. Dissolution of pure drug and it's solvates were performed by using USP II apparatus and it was observed that DMF solvate has the maximum dissolution amongst all solvates and pure drug. So, it is concluded that the antisolvent process has the significant effect on the dissolution of drug. Since all the techniques (DSC, SEM and XRD) used to assert the effect of the process on the dissolution

INTRODUCTION

Approximately 40% of drugs in the industry fall into the category of low solubility–high permeability (Class II), and low solubility–low permeability (Class IV). These classes have limited bioavailability of drugs due to their low solubility and dissolution rate (1).

The rate of oral absorption is frequently regulated by the rate of dissolution in the gastrointestinal tract for poorly soluble (BCS II drugs). As a result, a drug's solubility, dissolving behaviour, and permeability are essential factors in determining how bioavailable it is when taken orally. The development of water-soluble molecular complexes, drug micronization, solid dispersion, co-precipitation, lyophilization, microencapsulation, and the incorporation of drug solutions or liquid drugs into soft gelatin capsules are some of the significant formulation techniques used over the years to improve the dissolution profile and, in turn, the absorption efficiency and bioavailability of water-insoluble salts and

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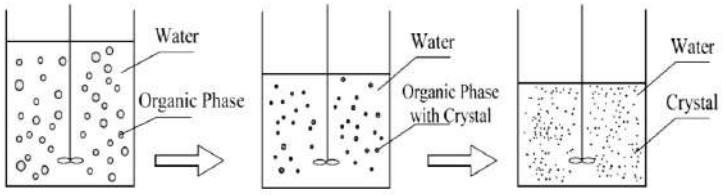
polymorphic forms (2). Poorly water-soluble active Pharmaceutical ingredients (APIs) may undergo incomplete dissolution in gastrointestinal fluids and thus be only partially absorbed into the systemic Circulation As it is reported, 40% of commercialized APIs and almost 70% of potential new drugs are poorly water-soluble (3) The main objective of this work they show the impact of antisolvent on the dissolution rate of the poorly water-soluble drug by formulating crystallization. The main objective of the present study is –

1. By determining the intrinsic dissolution rate of the drug.
2. By preparing crystals of nifedipine by using different antisolvent for the drug.
3. By characterizing the prepared crystals and
4. By formulating the appropriate dosage form of the prepared crystals of nifedipine.

MATERIAL AND METHOD

Anti-solvent crystallization for improving solubility, dissolution, and bioavailability of drugs with poor aqueous solubility. An anti-solvent crystallization technique is being used to prepare nanoparticles or microparticles for poorly water-soluble drugs at the research scale. This method can change the solid-state properties of pharmaceutical substances, including modifying crystal formation and particle size distributions. Therefore, various operating variables, their effect on the particle size of poorly water-soluble drugs in an anti-solvent crystallization, and problems related to anti-solvent crystallization when a solute can crystallize into two or more crystalline phases (a phenomenon known as polymorphism), but only one of them is wanted for product application, crystallization occurs when the solvent composition changes and favours one particular crystalline structure. Antisolvent crystallization has been utilized to crystallize a lot because of these traits



Preparation of recrystallization

Identification of compound

Identification of the compound was assured by UV-spectroscopy and FTIR spectroscopy.

UV spectroscopy analysis of drug

A standard solution (10mg/ml) of pure nifedipine was prepared by using 0.1N HCl, phosphate buffer, 7.4. The standard pure drug solution was scanned on UV spectroscopy (Shimadzu 1601). The peak with plateau was observed at 340 nm and used for further study.

FTIR Studies of Nifedipine drug

Fourier transform infrared spectroscopy is one of the powerful analytical techniques which offer the possibility of chemical identification. The technique is based on the simple fact that the substance shows selective absorption in the infra - red region. after the absorption of IR radiation, the molecules vibrate, giving rise to the absorption spectrum. FTIR measurement was analyzed on a perkin-Elmer FTIR spectroscopy. The FTIR spectrum was obtained in the mid-IR region of 400-4000 cm and recorded using the ATR (Attenuated reflectance technique). By interpreting the infrared absorption spectrum, the chemical bonds in a molecule. The Preformulation studies of the drug were performed and the result of the studies are given below.

Organoleptic evolution

Various sensory parameters such as colour, odour, taste, and appearance were studied for the drug. The results are shown below in the table no 8.2.1.

Name of drug	Appearance	Colour	Odour
Nifedipine	Powder	yellowish	odourless

Calibration Curve of nifedipine drug

It was observed that the drug followed Beer's Law very well at the concentration range from 1-10µg/ml.

Solubility

The solubility was performed in different pH for 24 hrs. The results are shown below in table no 8.4. and the solubility of the drug was found to be higher in highest at 1.2 pH

Stability in different pH

When the stability of the dug in different pH was studied then it was observed (Table 8.5) that drug was stable in pH 1.2 and pH 6.8 but it was found to be unstable at pH 7.4.

FTIR spectrum in the compatibility studies.

FTIR of individual polymer and drug was compared with FTIR of drug with different ingredient's mixture and absence of any new peak appeared if any, was considered for studies.

Differential scanning calorimetry (DSC)

DSC of the pure and recrystallized Nifedipine in different solvents was done by using a differential scanning colourimeter at a heating rate 10°C/min over a temperature range of 20-110°C. The sample was hermetically sealed in an aluminium crucible. Nitrogen gas was purged at the rate of 40ml/min to maintain inert atmospheres. The nifedipine(pure℃)drug the heat was 103.33(j/g)and the temperature was observed in 159.73and 179.94(℃)and highest peak are 10.989(mv) the ethanol heat is 111.508(j/g)temperature (160.06-180.94)maximum peak is 172.34℃ and highest peak was 9.484(mvv) the DMSO heat 103.33(j/g) temperature 159and 179.94(℃) maximum peak 172.075(℃) and highest peak 10.989(mvv) DMF heat 130.943(j/g) temperature162.60and 180.68(℃)maximum peak 171.97(℃)highest peak 7.153(mvv) are shown .

Scanning electron microscopy (SEM)

The morphology of the final crystal was detected by SEM and the average particle size of the crystals in different solvents are shown below in figure no 8.10.1,8.10.2,8.10.3,8.10.4. were found to be10µm.

X-Ray diffraction

The XRD pattern of pure drug, drug recrystallized in DMSO, DMF and ethanol are presented below in figure 8.12 to 8.14. XRD studies were used to identify the behavior of drug in different solvents. Prominent peaks in the graph show the packing arrangement of molecules or symmetry of the molecules in the particles and it was observed that pure drug was in amorphous form while recrystallized drug has more prominent and sharp peaks in the graph. Amongst all the DMSO has more crystalline structure than the ethanol and DMF.

DISSOLUTION STUDY:

When the dissolution of the various recrystallized drug was studied then the significant effect of the re-crystallization on the dissolution process was observed. More than 60-fold increase in the dissolution behavior of the drug in 0.1 N HCl was observed when compared with the water and more than 5-fold increase was observed in the 0.1NHCl. Well-formed crystals of almost 100 micrometer and 10 micrometer size were obtained when DSC data of before and after recrystallization were studied. When results of dissolution were correlated with the size of the drug before and after crystallization then it was found that the average size of drug before recrystallization was around 100 micro meter which was reduced to the 10 micrometres after the recrystallization and the smaller size of the recrystallized drug facilitated the dissolution of the drug. When the dissolution behaviour of drug was corelated with the XRD studies of the drug in DMF, DMSO and ethanol then it was observed that the more asymmetrically

molecules were arranged in the lattice were available more in the dissolution fluid. It was found that molecules were asymmetrically arranged in DMF when compared to the DMSO and ethanol. It was observed that the solvates are high energy structure and show more dissolution in the as compared to non-solvates. Which was further confirmed by the dissolution studies in 0.1 N HCl.

CONCLUSION

Dissolution the most important step before absorption of any drug, especially of BCS II drug. Nifedipine which belongs to the BCS II, is a dihydropyridine calcium channel blocker. It is chiefly used for the treatment of hypertension and belongs to a BCS II. Drug was identified chemically by UV and FTIR method while organoleptically by colour and odour and physical state. Maximum absorbance of the drug was found at 340 nm. Preformulation studies were conducted by measuring solubility in solutions (pH 1.2 N HCl, Phosphate Buffer pH 6.8 and 7.4) and was found to be 0.167, 0.104 and 0.084 mg/ml respectively. Drug was found to be stable in pH 1.2 and pH 6.8 while it was found unstable at pH 7.4. Intrinsic Dissolution rate of the pure drug was determined by using USP type II method in distilled water and 0.1 N HCl. Bulk Density and Tapped densities were found to be 0.5 g/ml and 0.66g/ml. Carr's was Index 24.24 while Hausner's Ratio was 1.32. which indicates drug has good flow properties. Recrystallization of the drug was done in DMF, DMSO and ethanol using water as antisolvent. Drug Excipient Compatibility Study was confirmed by FTIR method. Differential scanning calorimetry (DSC) of pure drug and it's solvates were done to confirm the crystalline structure of the and molecular symmetry was assured by XRD studies. Impact of the size of drug and it's solvates n dissolution was confirmed by SEM. Dissolution of pure drug and it's solvates were performed by using USP II apparatus and it was observed that DMF solvate has the maximum dissolution amongst all solvates and pure drug. So, it is concluded that the antisolvent process has the significant effect on the dissolution of drug. Since all the techniques (DSC, SEM and XRD) used to assert the effect of the process on the dissolution.

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