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Preparation and Characterization of Amlodipine Besylate Polymorphs

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ABSTRACT

The objective of the present work was to make different crystal forms of Amlodipine besylate. It was planned to prepare crystal forms using solvents of varying polarity and by change of phase and it was extended to characterize the prepared crystal forms using techniques like Scanning electron microscopy, IR spectroscopy, and Differential scanning calorimetry and/or X-ray diffractometry. Based on above these studies Amlodipine besylate pure was exisisted as Amlo-I, Amlo-II, Amlo –III and Amlo-IV forms were different in size and shape.

Keywords: Amlodipine besylate, Scanning electron microscopy, IR spectroscopy and Differential scanning calorimetry and/or X-ray diffractometry.

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INTRODUCTION

One of the most important physical factors, which affect bioavailability, and therapeutic efficacy of a drug is the existence of active ingredients in various crystal forms with varying internal structure and physicochemical properties. Solids may be prepared in a particular crystal form via appropriate manipulation of conditions of crystallization like nature of solvent, temperature, rate of cooling etc[1]. These crystal forms of a given solid differ from each other with respect to many physical properties such as solubility, dissolution rate, true density, crystal shape, compaction behavior and flow properties. The present work was undertaken with the aim to study crystal forms of Amlodipine besylate, a new class of widely used anti-hypertensive agents.

MATERIALS AND METHODS

Amlodipine besylate pure was obtained Reddy's Laboratories, Hyderabad. The various solvents used for preparation of crystals were Distill water, Ethyl acetate, Ethanol, Di-methyl formide, Acetone, Acetonitrile, Acetic acid, Ammonia, Benzene, Chloroform, Di-methyl sulfoxide, (Chempure Laboratories, Chennai).

Preparation of Crystal Forms of Amlodipine besylate from Different Solvents

The drug (0.5g) was dissolved in respective solvents (20ml) to check its solubility. To this solution, another weighed amount of Amlodipine besylate (2.5-3.5g) was added and refluxed only with Distill water, Ethyl acetate, Ethanol and DMF (100-150ml), for 20 minutes. This solution was filtered through whatmann filter paper and concentrated by recovery of the solvent to one third of its original volume and kept for crystallization at room temperature to afford well-defined crystals of Amlodipine besylate. The crystals obtained were collected by filtration, dried under vacuum for 24 hours and stored in well closed container.

Characterization of Crystals

Scanning Electron Microscopy[2,3]

All the crystals so prepared were viewed under scanning electron microscopy were taken for characteristic studies. For the external morphology studies, the crystals were visualized using scanning electron microscopy (SEM JEOL JSM-6701 F,JAPAN) operating at 15kv. The samples were mounted on a metal stub with double adhesive tape and coated with platinum/palladium alloy under vacuum. The shape and surface characteristic of the microspheres was observed in electron micro analyzer and photographs.

IR Spectroscopy[4]

The crystal samples (2-2.5 mg) were triturated with dried potassium bromide (100 mg) using agate

mortar and pestle. These quantities were usually sufficient to give a disc of 13 mm diameter and a spectrum of suitable intensity. The mixture after grinding into a fine powder was spread uniformly in a suitable die and compressed into a pellet form at a pressure of about 10kg/cm^1 for three minutes by using hydraulic press. The resultant pellet was mounted in a suitable holder in the FT-IR spectrophotometer and full range spectra of all crystals were recorded form 4000 cm^{-1} to 400 com^{-1}.

Differential Scanning Calorimetry[5,6]

The instrument was calibrated using Indium as standard. The sample (2-10mg) was weighed accurately in aluminium pan and sealed hermetically using a crimper. Thermograms were obtained by heating the encapsulated samples at a constant heating rate of 5^{o}C/min with chart speed of 5 mm/min under an atmosphere of nitrogen. The exact peak temperatures, melting point and heat of fusion were determined. The temperature range for the scan was 30^{o}C to 450^{o}C for all the samples.

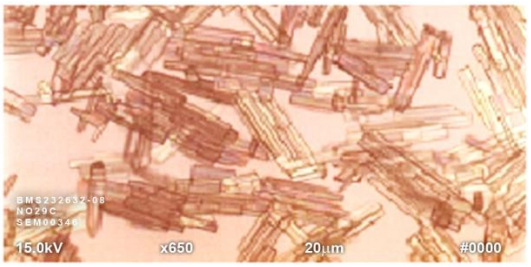
Powder X-Ray Diffraction Spectroscopy[7, 8]. All crystal samples were ground and screened through 100 meshes. The X-ray diffraction pattern was recorded using Phillips Analytical automatic powder differactometer at 30mA, 40KV. The samples were scanned at a temperature 25^{0}C at the diffraction angle 2 θ over the range of 5-40^0.

RESULTS AND DISCUSSION

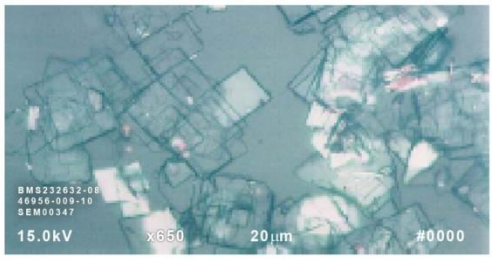
Photomicrographs showed the prepared crystals of **Amlo-I, Amlo-II**, **Amlo-III and Amlo-IV** to (shown in figure 1) be of different shapes and sizes.Melting points of the crystals were found to be same except**, Amlo-II and Amlo-IV**. From DSC data (Table 1), it is observed that there is a slight change between **Amlo-I and Amlo-III** in onset of peak (192.52^{oC}; 194.69^{oC}) heat of fusion (137.36^{oC}; 160.42^{oC}).

Table 1: Melting Point, DSC data and shapes of Amlodipine besylate crystal forms

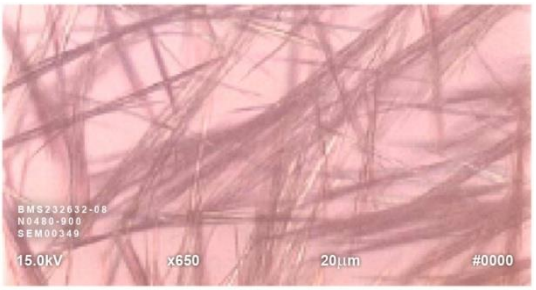
Crystal Form	Solvent used	Melting point (^{o}C)	On set of peak	Heat of fusion points (^{o}C)	Peak fusion point(^{o}C)	Shape of Crystal
Amlo - I	Distilled water	191-192	192.52	137.36	204.80	Bricks like crystals
Amlo -II	Ethyl acetate	224-225	224.03	144.74	229.41	Rectangular like crystals
Amlo -III	Ethanol	194-195	194.69	160.42	207.78	Needle like crystals
Amlo - IV	DMF	252-253	252.11	157.23	256.19	Prism Like crystals



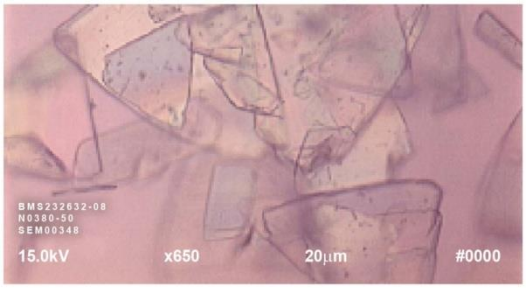
From water



From Ethyl acetate



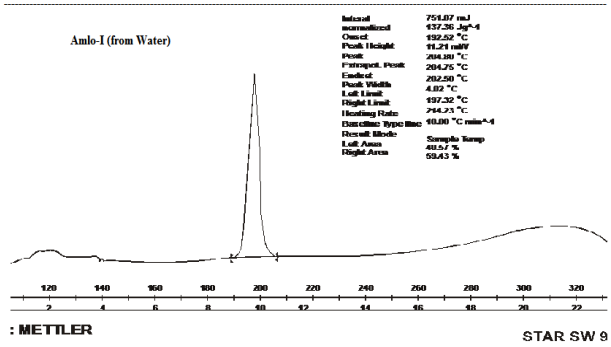
From Ethanol



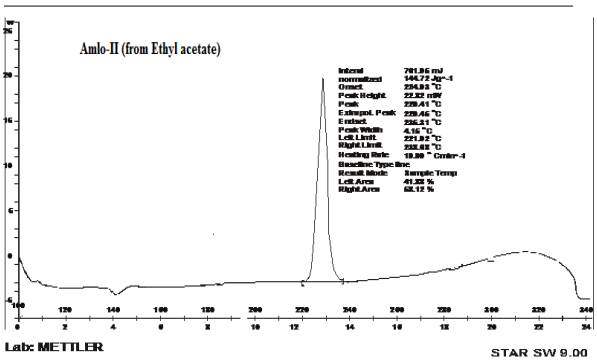
From DMF

Figure 1: SEM Photographs of Amlodipine besylate Crystals from Different Solvents

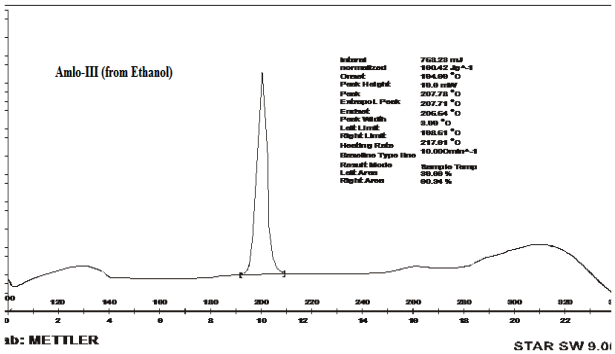
But there was a significant difference in onset of peak (224.03$^{°C}$, 252.11$^{°C}$) and heat of fusion (144.72$^{°C}$ and 157.23$^{°C}$) for **Amlo-II** and **Amlo-IV**. From the above observation it was concluded that and **Amlo-II, and Amlo-IV** are having significantly different chemical and crystal structures. But Amlo-**I and Amlo-III** structure varies slightly.



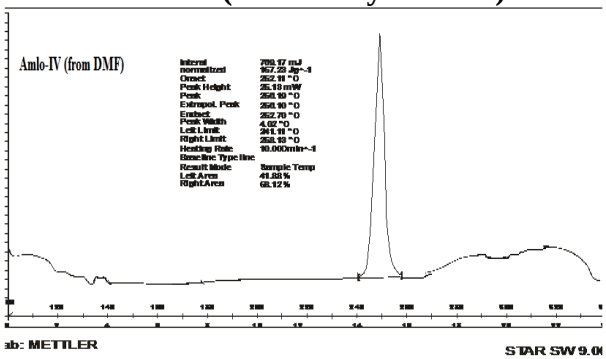
Amlo-I (From Distill Water)



Amlo-II (From Ethyl acetate)



Amlo-III (From Ethanol)



Amlo-IV (From DMF)

Figure 2: DSC Spectras of Amlodipine besylate Crystals from Different Solvents.

IR spectra of the pure drug (Amlodipine besylate), prepared crystal (Amlo-I,Amlo -II, Amlo -III and Amlo-IV)were recorded using potassium bromide disc method in shimadzu FT-IR instrument(Japan).It was observed that there was no incompatible reactions/ interaction between the drug Amlodipine besylate and the solvents used. Which was clearly showed in the spectra whose vibrational frequencies were tabulated as follows in (Figure 3).

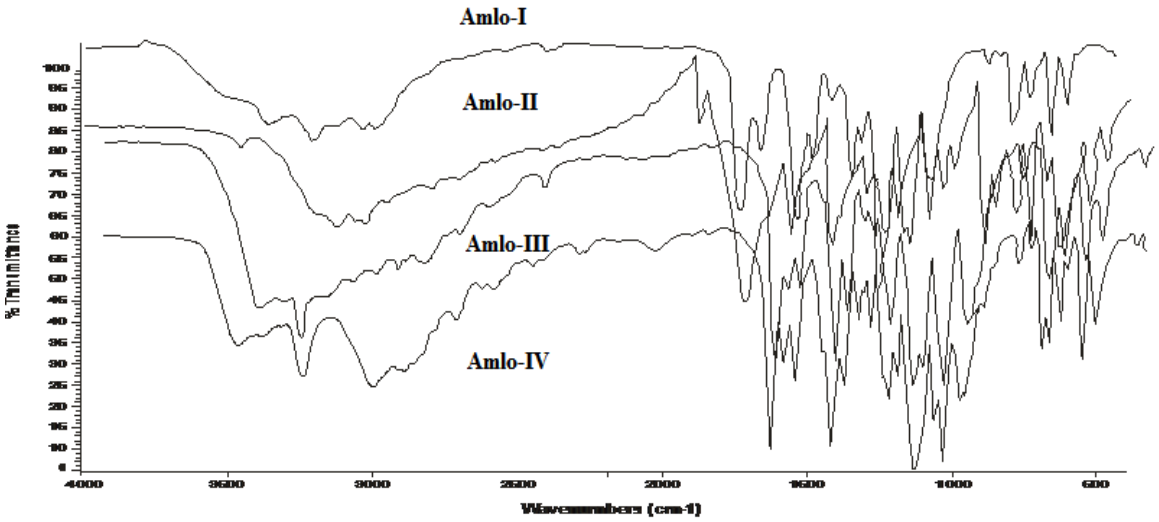
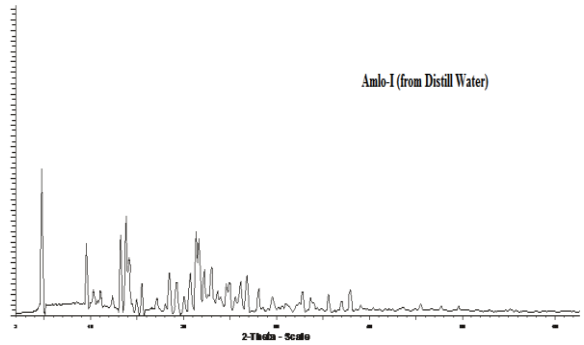
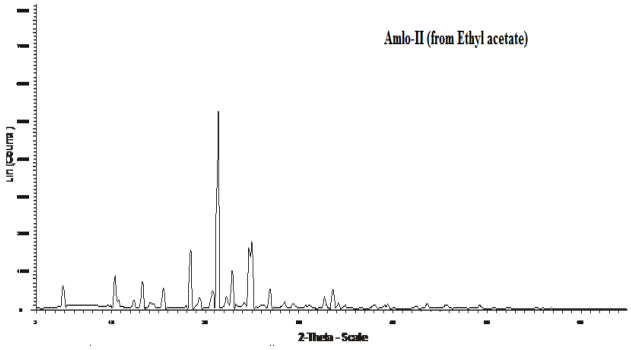


Figure 3: FTIR Comparison Spectra of Amlo-I, II, III & IV

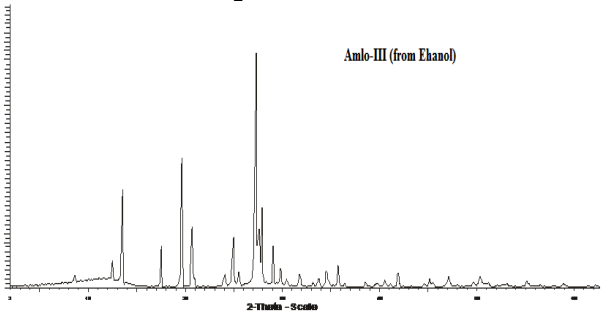
Considering powder X-ray diffractometry (PXRD) to be the ideal technique for characterizing polymorphs, all the crystal forms were submitted for PXRD studies.



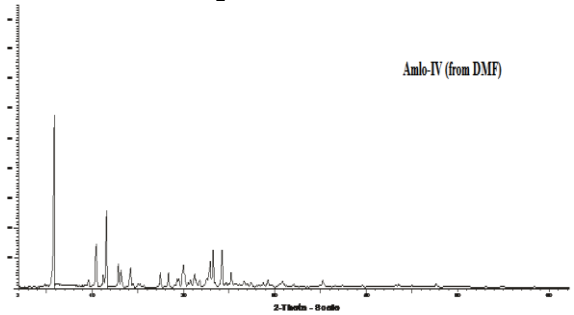
XRD Spectra of Amlo-I



XRD Spectra of Amlo-II



XRD Spectra of Amlo-III



XRD Spectra of Amlo-IV

Figure 4: XRD Spectras of Amlodipine besylate Crystals from Different Solvents.

In PXRD Amlo-I crystals was prepared in amphichroic polar solvent (water) which shown high intensity at 4.8, 14.0°2θ, High intensity scattering angle of Amlo-II (Ethyl acetate) shown at 21.5 & 18.0°2θ, Amlo-III (Ethanol) shown intensity at scattering angle 27.2, 13.5°2θ and Amlo-IV (DMF) showed high intensity at scattering angle 5.8 and 11.5°2θ. Shown in (Figure 4). Pure Amlo PXRD data was compared with the reported PXRD data of Amlo-I, Amlo-II, Amlo-III and Amlo-IV. Pure Amlo shows entirely different pattern as well as intense lines at scattering angle 5.5, 9.4, 24.2, 22.2°2θ.From the PXRD studies, it was observed that there is different crystal forms existed in all the polymorphs when compared to the pure drug.

CONCLUSION

The present work was undertaken with the aim to study crystal forms of Amlodipine besylate by crystallization from single solvent method (from Distill water, Ethyl acetate, Ethanol, and DMF). Efforts were made to characterize the crystalline materials by Melting point, Scanning Electron Microscopy, DSC, FT-IR and XRD. In this characterization melting point or DSC data did not shown significant results. But Scanning electron microscopy photographs (Figure: 01), XRD spectra of all the crystal forms showed a significant variation in their shape between Amlo-I, II, Amlo-III (Ethanol) shown intensity at scattering angle 27.2, 13.5°2θ and Amlo-IV (DMF) showed high intensity at scattering angle 5.8 and 11.5°2θ. Shown in (Figure 4). An IR spectrum of the pure drug (Amlodipine besylate) and prepared crystal was given in (Figure 3). From this it was concluded that there is no incompatible reactions/ interaction between the drug Amlodipine besylate and the solvents.

REFERENCES

1. Matsuda Y, Tatsumi E. Physicochemical characterization of furosemide modifications. Int J Pharm 1990; 60:11–26.
2. Singh D, Marshall PV, Shilds L, York P. Solid-state characterization of chlordiazepoxide polymorphs. J of Pharm Sci 1998; 87: 655–662.
3. Otsuka M, Hasegawa H, Matsuda Y. Effect of polymorphic forms of bulk powders on pharmaceutical properties of carbamazepine granules. Chem Pharm Bull 1999; 47: 852–856.
4. Tang XC, Pikal MJ, Taylor LS. The effect of temperature on hydrogen bonding in crystalline and amorphous phase in dihydropyrine calcium channel blockers. Pharm Res 2002; 19: 484–490.

5. Romero S, Escalera B, Bustamante P. Solubility behavior of polymorphs I and II of mefenamic acid in solvent mixtures. Int J Pharm 1999; 178: 193–202.
6. Vippagunta SR, Brittain HG, Grant DJW. Crystalline solids. Adv. Drug Deliv. Rev 2001; 48: 3– 26.
7. Suryanarayanan R, Byrn SR. Characterization of the solidstate. Adv. Drug Deliv. Rev 2001; 48: 1 –136.
8. Chakravarty P, Alexander KS, Riga AT, Chatterjee K. Crystal forms of tolbutamide from acetonitrile and 1-octanol: effect of solvent, humidity and compression pressure. Int J Pharm 2005; 28: 335–348.