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Der Pharmacia Sinica, 2012, 3 (6):610-615

Der Pharmacia Sinica
ISSN: 0976-8688
CODEN (USA): PSHIBD

Growth and characterization of drug crystals from sodium meta silicate

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ABSTRACT

An Active Pharmaceutical Ingredient (API) Aspirin was crystallized from Sodium Meta silicate (SMS) by gel growth method for the first time. The growth parameters and the various properties of the drug crystals are observed and characterized by different instruments. The lattice parameters were determined by single crystal X-ray diffraction studies. FTIR and UV - Vis spectral studies have also been carried out to identify the functional groups present and the rate of absorbance of the drug crystal. Thermal analysis by TG-DTA shows good thermal stability. Dielectric studies reveal that the dielectric constant decreases with increase in frequency.

Key words: Active Pharmaceutical Ingredient, drug crystals, growth parameters, characterization, analysis.

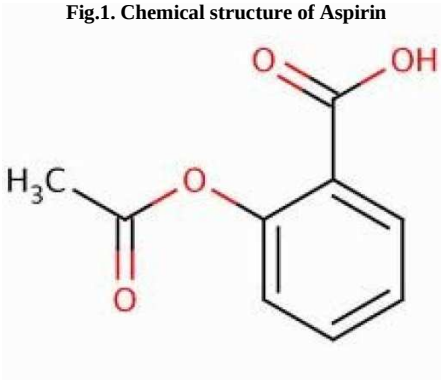
INTRODUCTION

Aspirin [Acetyl salicylic acid - ASA] is well known as a non – steroidal anti – inflammatory (NSAID) drug, which is the active ingredient of many oral medicines in tablets. Aspirin consists of some metal binding complexes, such as acetyl, phenyl and carboxylic groups. These functional groups are responsible for various medicinal activities and also it will interact with the metal ions present in water. Today, Aspirin is one of the most widely used medicines as an analgesic (pain killer), antipyretic (fever reducer), anticoagulant (blood thinner) and an antiplatelet (antiaggregant) drug. Most of the drugs are delivered to patients in crystalline form [1]. Crystallization of API is not only an important art but also provides the knowledge about physical properties of crystalline nature such as crystal form, shape and size. Owing to the biological and medicinal importance of Aspirin, it was crystallized from SMS by gel method. This research work system can be employed at various stages of drug development in pharmaceutical preparations an d applications. Because APIs and their salts are isolated and purified by crystallization in the final step of synthetic process.

MATERIALS AND METHODS

Materials:
Pharmaceutical grade of Aspirin was supplied by M/S. Sri Krishna Laboratories, Hyderabad, India. Commercially available sodium meta silicate and ethanol was purchased from M/S. Merck India Ltd, Mumbai.

Fig.1. Chemical structure of Aspirin



Methods:

Crystal growth from gel:

Gel method gained enormous role in crystallization due to its simplicity, feasibility and versatility. A gel is a two-component system, semi solid in nature and rich in liquid. Diffusion takes place through fine pores. Sodium Meta silicate gel is widely used as a crystal growth medium in most of the growth experiments, since it is inert [2] we preferred to crystallize Aspirin in this nature.

Preparation of gel for crystal growth:

The gel medium prevents turbulence and helps to form good crystals by providing a frame work of nucleation sites [3]. Silica gel prepared from an aqueous solution of SMS (N $a_2SiO_3.5H_2O$) of specific gravity 1.04 gm/cm^3. T he pH and concentration of the gel medium were adjusted to get best conditions for crystal growth. Aspirin was mixed with ethanol. This solution was added to gel growth medium and it was carried out at room temperature (≈28℃). 250ml beaker was used as crystal growth vessels instead of test tubes. Bunched rod shaped and isolated needle shaped pink color crystals were formed at the bottom of the beaker. The crystals are collected carefully and dried after a growth period o f 5-7 weeks.

Fig.2. The as grown drug crystal

The yield of drug crystal was 80 %. The dimensions of the grown crystals are 9 ×2×2mm^3 and it was shown by different snapshots in fig (1). The grown crystal was observed to be thermally stable, non – hygroscopic and not decomposed when exposed to air at ambient temperature [4].

RESULTS AND DISCUSSION

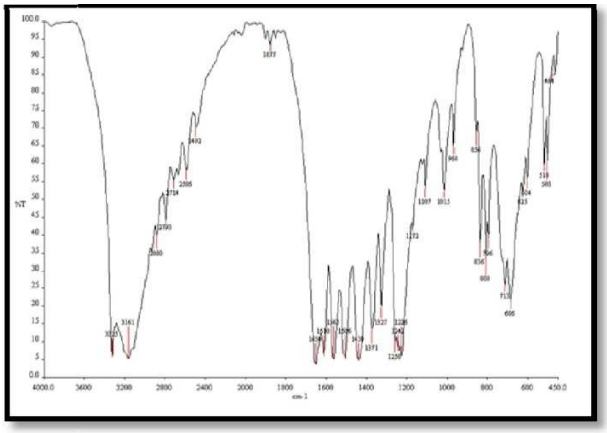
Characterization of solid phase drug crystal:

The physicochemical properties of the organic pharmaceutical crystal are important in the drug discovery and development phase. The general methods for the characterization of crystalline phase for these properties are single crystal X-Ray Diffraction, FTIR, thermal analysis. These methods have been reviewed in detail by several authors [5,6,7]. All these characterization were done and the results will be discussed herein detail.

Single X – ray diffraction studies:
The most valuable information about the molecular and crystalline structure in solid phase nature is determined by single crystal X -ray diffraction [8,9]. Single X –Ray diffraction analysis for the grown crystal was carried out us ing an ENRAF NONIUS CAD - 4 X-Ray diffractometer. From the diffraction analysis the unit c ell parameters for the grown crystals was a = 7.09 Á, b = 9.38 Á, c = 11.73 Á, β = 97.38°, V= 777 Á^3 and space group $P_{21/c}$. The as grown bi molecular crystal belongs to monoclinic system. This form of drug compound is thermodynamically stable at room temperature [10] which is one f the essential properties during the manufacturing process in pharmaceutical industry.

FTIR analysis:
Drugs which owe their pharmacological effects to chemical interactions with metal complexes are likely to have special effects. The study of this molecular interaction of drugs in solid phase [11] provides useful information in pharmaceutical and medicinal chemistry. Spectroscopy is the most powerful tool available fo r the analysis of a wide range of compounds such as functional groups conformation, environment of organic compounds and finger print of molecular solid [12,13]. The FTIR analysis of the grown drug crystals was recorded between 4 50 and 4000 cm^{-1} using KBr pellet technique by B RUKKER IFS 66V spectrometer and the resultant spectrum is shown in figure (3).

Fig. 3. FTIR Spectrum of the grown crystal



The bands at 3161 cm^{-1} and 14 41 cm^{-1} established the presence of ammonium ion, whereas at 3324 cm^{-1} and 1654 cm^{-1} is due to alkenyl C-H and C= C stretch. The absorption peaks at 2926 cm^{-1} and 2792 cm^{-1} indicates in the presence of carboxylic acid C = O stretch. The presence of aromatic ring skeletal vibrations is observed at 1506 cm$^{-1.}$ The peaks corresponding to 1370 and 1327 cm^{-1} bring forth CH_3 rocking and the peaks at 1259 cm^{-1}, 1242 cm^{-1} and 1226 cm^{-1} shows C=O stretch respectively. The ab sorption peaks between 1172 cm^{-1}and 1015 cm^{-1} arise due to the presence of phenol O-H stretching.

UV – VIS spectral studies:
UV – Vis spectral data is used to measure the transparency and concentration of the crystal. Optical absorption studies for the grown biological crystals were carried out using Varian Cary - 5E spectrometer in the range of 500nm – 2500nm. Fig (4) shows the plot of absorbance verses wave length spectrum.

The spectrum indicates that the absorbance behavior in the entire UV, Visible a d IR region. The maximum absorbance is at λ=250nm with nearly 80% of transmittance. After this the rate of absorbance decreases gradually up to 800nm to 1500nm which enables the molecular concentration level of the crystal.

Thermal analysis:
Thermal Analysis (TA) is the most precise method used in the preformulation and development of drugs [14,15] that the change of temperature may influence the stability of the drug molecules. Thermal analysis of the drug crystal was carried out using NETZSCH STA 09 C/CD model analyzer. The powered sampl e weighing 9.390mg was used for this analysis in the nitrogen atmosphere and the thermogram is depicted in fig (5) and fig. (6).

Fig. 4. Optical absorption spectrum of the grown crystal

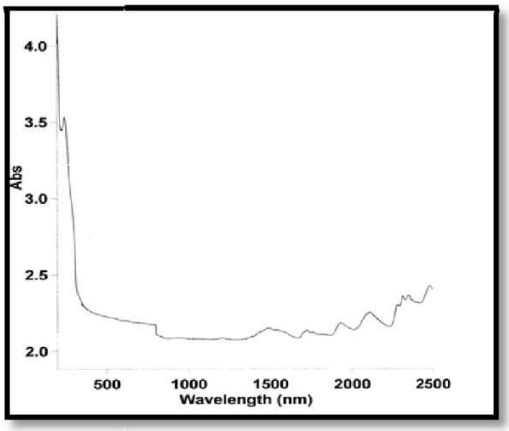


Fig. 5. T GA Spectrum of the grown crystal

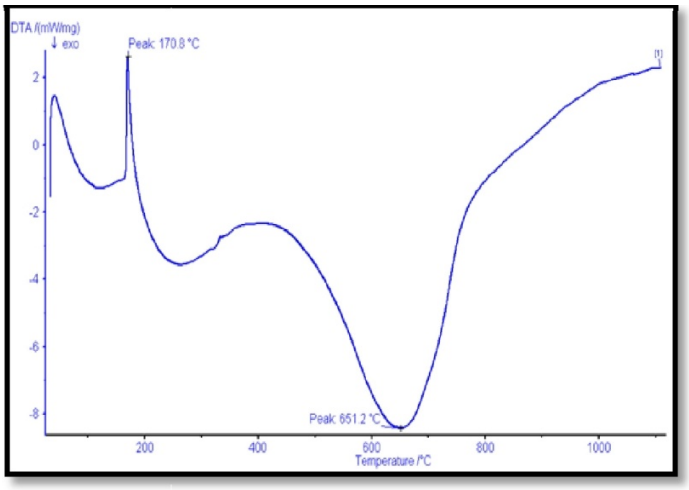
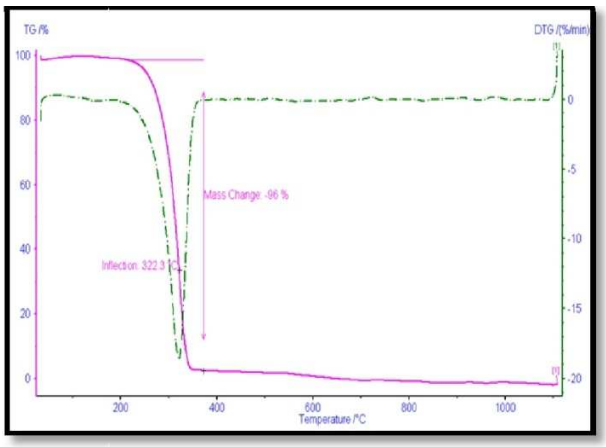


Fig. 6. DT A Spectrum of the grown crystal



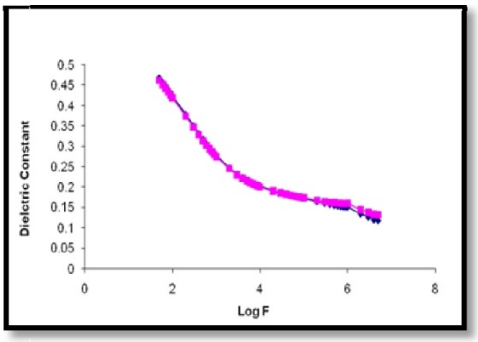
From the thermal studies the crystal can retain its texture up to 220°C, after that it starts to decompose gaseous molecules like CO2 and NH gradually by the loss of mass in temperature range between 230°C - 400°C. The decomposition illustrates almost 100% f weight loss at 680°C.

The DTA thermogram also reveals that the exothermic peak at 170.9°C may assign to solvent molecule evaporation which enables that the compound can be used for many applications below its melting point [16] and ensuring the production quality.

Dielectric studies:

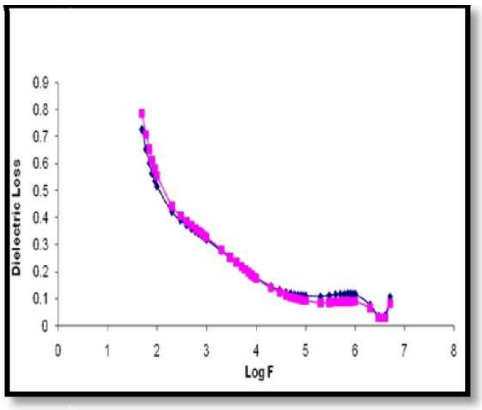
Dielectric measurements were performed on the as grown crystals using a HIOKI HITESTER model 3532 – 50 LCR meter. The sample of dimension 2.5×2×2 mm^3 has been placed inside a dielectric cell whose capacitance was measured at different temperatures for different frequencies. The techniques use d for the measurement of dielectric constant are either reflection coefficients or resonant frequencies.

Fig. 7. Variation of dielectric constant



The dielectric constant and dielectric loss decreases with increase in frequency was shown in fig (7) and fig (8).

Fig.8. Variation of dielectric loss



CONCLUSION

As a result of this research study, it was found that ASA was crystallized in SMS from small, medium and big sizes at room temperature by gel growth method. The single crystal X – ray diffraction results shows that the crystal belongs to monoclinic system. The FTIR spectrum confirms both Aspirin and SMS compounds were present in the sample. From the UV spectrum results that the cut off wavelength of the drug crystal is 250nm and the thermal analysis shows the stability, decomposition and melting points were 220°C, 97% at 400°C and 170.8°C respectively. Dielectric studies indicate that the dielectric constant decreases with increase in frequency and very low dielectric loss illustrates very high purity of the crystal.

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