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Evolution of Crystalline Line Solids and its Tools

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ABSTRACT

Morphological and thermodynamic transitions in drugs as well as their amorphous and crystalline content in the solid state have been distinguished by thermal analytical techniques, which include dielectric analysis (DEA), differential scanning calorimetry (DSC), and macro-photomicrography. These techniques were used successfully to establish a structure versus property relationship with the United States Pharmacopeia standard set of active pharmaceutical ingredient (API) drugs. A distinguishing method is the DSC determination of the amorphous and crystalline content which is based on the fusion properties of the specific drug and its recrystallization. The DSC technique to determine the crystalline and amorphous content is based on a series of heat and cool cycles to evaluate the drugs ability to recrystallize. To enhance the amorphous portion, the API is heated above its melting temperature and cooled with liquid nitrogen to -120 C (153 K). Alternatively a sample is program heated and cooled by DSC at a rate of 10 C min-1 . DEA measures the crystalline solid and amorphous liquid API electrical ionic conductivity. The DEA ionic conductivity is repeatable and differentiates the solid crystalline drug with a low conductivity level (10-2 pS cm-1) and a high conductivity level associated with the amorphous liquid (106 pS cm-1). The DSC sets the analytical transition temperature range from melting to recrystallization. However, analysis of the DEA ionic conductivity cycle establishes the quantitative amorphous and crystalline content in the solid state at frequencies of 0.10–1.00 Hz and to greater than 30 C below the melting transition as the peak melting temperature. The amorphous content is inversely proportional to the Ea where the Ea for the crystalline form is higher and lower for the amorphous form with a standard deviation of ±2%. An alternate technique to determine amorphous and crystalline content has been established for the drugs of interest based on an obvious amorphous and crystalline state identified by macro-photomicrography and compared to the conductivity variations. This second ‘‘empirical method’’ correlates well with the ‘‘activation energy’’ method.

1. Introduction

Riga et al. contemplated the broad uses of dielectric investigation (DEA) including conditions of issue as formless/crystalline. They portrayed medications, excipients, transdermal patches, starches, proteins, amino acids, engine oil dispersants, and surfactants just as electro rheological liquids utilizing A.C. electrical properties over a wide scope of frequencies [1]. The significance of the shapeless state when examining bioavailability, disintegration, and the advancement of ineffectively water dissolvable APIs has become altogether over the ongoing years [2, 3]. There are two types of solids: smooth and crystalline structures [4]. Smooth structures or nebulous strong structures by and large exist in an assortment of mechanical fields or items, for example, polymers and plastics, materials, nourishments and pharmaceuticals, and in the production of semiconductors, earthenware production, metals, and optical materials [2, 3]. With reference to a crystalline strong, an indistinct strong can be characterized as a substance with short-run atomic request; conversely a crystalline strong has long-extend request [2]. Thus, some shapeless structures are considered as fluids in spite of the fact that they can cement by the evacuation of warm vitality or a dissolvable in a manner that keeps away from crystallization [5]. In pharmaceutical research, the shapeless type of a pharmaceutical strong has been the most significant part of medication improvement. The hugeness of nebulous solids is by and by consistently expanding because of their incentive to the pre-clinical detailing researchers and as a rule to the pharmaceutical business because of different points of interest [3, 6, 7]: (I) a constant increment in the advancement of various insoluble APIs; these shiny medication mixes are extraordinary dependent on their strategies for generation and screening [8], (ii) the developing consideration in administrative assessment and unmistakable monetary parts of pharmaceutical solids improvement [9], and (iii) the various polymorphs of APIs including the shapeless structures have distinctive interconvertible physical and concoction properties [10] which show diverse dissolvability and compressibility attributes. Preparing of an undefined medication substance is generally straightforward, and simple when contrasted with crystalline medication generation [2, 3].

Indistinct structures can be delivered by an assortment of pharmaceutical systems, for example, granulation, compaction, stop and splash drying, dissolve extinguish cooling, and dissolvable vanishing strategy. These nebulous structures can be utilized for better dissolvability, disintegration, and bioavailability [6, 11, 12]. The indistinct stage has higher vitality with higher synthetic reactivity and for the most part is less steady both physically and synthetically than that of the comparing crystalline stage. The security of the shapeless

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structure is the primary issue when put away at temperatures near the glass change temperature (Tg). The glass progress temperature is a key trademark property of undefined materials. Measurement of the shapeless portion of an API can be better comprehended by deciding the warmth limit change related with the Tg [13]. In pharmaceuticals, indistinct solids have a few valuable properties and are utilized as the two API and excipients [3]. A portion of the valuable properties are a higher water dissolvability, higher disintegration rate [14] (i.e., no grid vitality, which is a thermodynamic boundary to disintegration) [15], and better pressure attributes when contrasted with the crystalline structures [2, 3].

Crystalline solids are crystalline

The crystalline idea of materials, for example, salt or precious stone is plainly evident to the unaided eye. Things being what they are, notwithstanding, that gems happen more regularly than anticipated in nature and numerous different materials which are not clearly crystalline in appearance have a long go crystalline structure. For sure metals and semiconductors and numerous different covers beside just precious stone and salt embrace crystalline structures. The key property of crystalline solids is their characteristic evenness which emerges in light of the ordinary plan of their cores. It is intriguing to note, notwithstanding, that the real meaning of the term gem given by the International Union of Crystallography (IUC) is to some degree more extensive than an exchange dependent on periodicity of the particles would suggest. In particular, IUC characterize a precious stone as "any strong having a basically discrete diffraction outline". This definition, which is plainly to some degree poorly characterized, has emerged principally to represent the perceptions, from the 1980s, of quasiperiodic gems, supposed "quasicrystals" [1]. In this manner intermittent precious stones, which we will concentrate on here, are only a subset. How the cores are orchestrated prompts the gem structure which is the novel course of action of particles in a precious stone made out of a unit cell: a lot of iotas organized with a specific goal in mind which is intermittently rehashed in three measurements on a cross section. The unit cell is given regarding its grid parameters, the length of the unit cell edges and the edges between them. Crystallographers are adroit at arranging, tallying, and systematizing gem types as per their balance and precious stone framework. We won't wander into the universe of crystallography but to state that for a general precious stone structure in which objects of subjective balance are deciphered on a supposed Bravais grid that there end up being 230 diverse evenness bunches that a cross section can have, known as the 230 space gatherings. At the point when the article to be deciphered (the "premise") is totally symmetric, for example, a solitary iota is, there end up being fourteen space gatherings (the fourteen Bravais grids) falling into seven precious stone structures (cubic, tetragonal, orthorombic, monoclinic, triclinic, trigonal, and hexagonal). Luckily, for present purposes, we don't have to stress over each of the 230 space gatherings or even every one of the fourteen Bravais cross sections since natural solids under standard conditions embrace few structures. Without a doubt over 70% [2] of every single natural strong embrace one of the accompanying four gem structures: • Body-Centered Cubic (bcc): This is a straightforward cubic structure with iotas at the side of a shape alongside an extra particle at the focal point of the 3D square (Fig. 1(a)). The soluble base metals and numerous early change metals embrace this structure;

• Face-Centered Cubic (fcc): Again this is a basic cubic structure yet now with an extra particle at the focal point of each square face (Fig. 1(b)). Most late change and respectable metals receive this structure just as the dormant gas solids and a portion of the soluble earth components;

• Hexagonal Close Packed (hcp): This comprises of two interpenetrating straightforward hexagonal cross sections as appeared in Fig. 1(c). A few progress metals embrace this structure;

• Diamond: This comprises of two interpenetrating face-focused cubic cross sections (Fig. 1(d)). The gathering IV components (C, Si, Ge, and Sn) frequently crystalize in this structure.

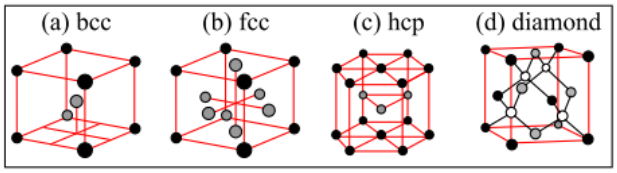

FIG. 1: Illustration of the four types of crystal structure most commonly adopted by elemental solids

Another central property of solids is their cohesive energy, Ecoh. This is the energy needed in order to rip a sample apart into a gas of widely separated atoms, as illustrated schematically in Fig. 2.

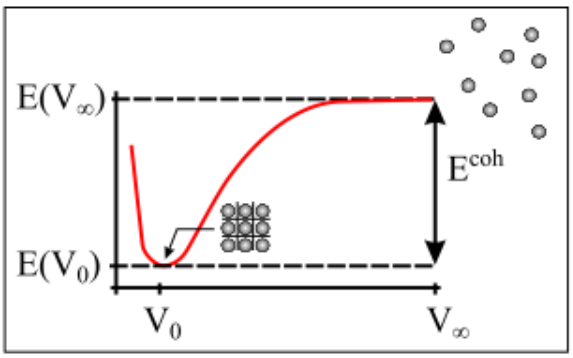

FIG. 2: Schematic illustration of a typical energy-volume equation of state for a solid

If {V} denotes some structural parameter characteristic of a given crystal, such as, for example, the unit cell volume, and {Vo} represents the value at the equilibrium crystal structure, we thus have

$$E^{\mathrm{coh}} = -\left(\frac{E(\{\mathbf{V_o}\})}{M} - \frac{E(\{\mathbf{V}\}\to\infty)}{M}\right).$$

Here E is the vitality of the strong, and M the quantity of iotas in the precious stone. The vitality that is utilized in (1) is the all out electronic vitality (dismissing the zero point vitality in this definition). The absolute electronic vitality is a huge negative number, which prompts a positive Ecoh in the definition above. Durable energies of basic solids extend from minimal in excess of a couple meV per molecule for the dormant gases to just shy of 9 eV for each particle for tungsten.

On the off chance that one thinks about the variety of the vitality with volume, at that point, since both vitality and volume

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are state capacities, what we have is a condition of state (EOS) for the gem. Conditions of state for natural solids all the time resemble the sketch in Fig. 2. The contrast between one material and the other is dictated by varieties in the profundity, area, and shape of the base. Numerous valuable expository articulations for the utilitarian type of the EOS for solids have been created. The most famous of them being the EOS due to Murnaghan [3], which is given by:

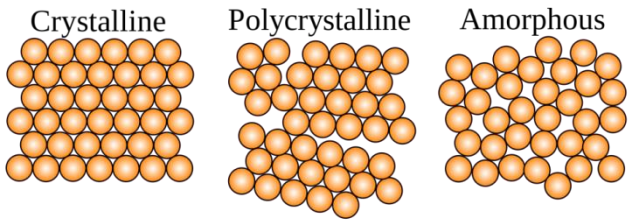
$$\frac{E(V)}{M} - \frac{E(V_o)}{M} = \frac{B_o V}{B_o'(B_o'-1)}\left[B_o'\left(1-\frac{V_o}{V}\right)\right]$$

where the new quantities above are, Bo, the bulk modulus, and, B0 o, its pressure derivative. The bulk modulus of a substance essentially measures its resistance to uniform compression and is defined as:

$$B_o = V\frac{\partial^2 E(V)}{\partial V^2}\bigg|_{V=V_o} .$$

Crystalline Solids

These are the most widely recognized kind of solids. Their attributes are what we partner solids with. They are firm, hold a distinct and fixed shape, are inflexible and incompressible. They for the most part have geometric shapes and level appearances. What's more, models incorporate jewels, metals, salt and so on. To comprehend precious stones we should comprehend their structure. The game plan of particles in a crystalline strong is in an organized manner. These articles are organized in a rehashing example of a three-dimensional system. This system is known as a Crystal grid and the littlest unit of a precious stone is a Unit Cell. On the off chance that you see the X-beam of a gem this unmistakable game plan of the unit cells will be plainly obvious. The spaces between the particles are less because of high intermolecular powers. This outcomes in gems having high liquefying and breaking points. The intermolecular power is additionally uniform all through the structure. Precious stones have a long-go request, which means the game plan of molecules is rehashed over a huge span.



Amorphous Solids

Indistinct solids are unbending structures yet they come up short on a well-characterized shape. They don't have a geometric shape. So they are non-crystalline. This is the reason they don't have edges like precious stones do. The most widely recognized case of a nebulous strong is Glass. Gels, plastics, different polymers, wax, slight movies are likewise genuine instances of indistinct solids. This variety in qualities of solids happens because of the course of action of their atoms. Here the particles of issue don't shape the three-dimensional grid structure that we find in solids. Some normally happening indistinct solids have debasements that keep such a structure from framing. So they have a short request plan of atoms. Formless solids break into uneven pieces with unpredictable edges. Also, they don't have any unmistakable game plan or state of atoms. so they can't be distinguished by their structure as gems.

Distinction among Crystalline and Amorphous Solids

- Crystals have a precise plan of their constituent particles. In correlation, undefined solids have no such game plan. Their particles are arbitrarily composed.
- Crystals have a particular geometric shape with clear edges. Indistinct solids have no geometry in their shapes
- Crystalline solids have a sharp softening point on which they will liquefy. A nebulous strong will have a scope of temperature over which it will soften, yet no positive temperature all things considered
- Crystals have a long request game plan of their particles. This implies the particles will demonstrate a similar course of action uncertainly. Shapeless solids have a short request course of action. Their particles demonstrate a great deal of assortment in their plan.
- Crystalline solids cleavage (break) along specific focuses and headings. Nebulous solids cleavage into uneven parts with worn out edges.
- Crystals are otherwise called True Solids, while another name for Amorphous Solids is Super-Cooled Liquids.

2. Methodology

Two epic DEA conventions were created to deciding the nebulous and crystalline substance in pharmaceutical medications. The main strategy is "The exact technique." It is semiquantitative strategy that depends on the watched huge electrical conductivity contrast between the nebulous fluid (107 pS cm-1) and crystalline strong (10-2 pS cm-1). The subsequent technique is the "actuation vitality strategy" and is increasingly quantitative in nature. In this technique, the actuation vitality, Ea (J mol-1), is determined from the DEA ionic conductivity. It depends on the way that the relative Ea for the electrical reactivity (charging or charge transport) in the strong condition of the formless stage is higher and then again the Ea is lower (regularly 30–110 J mol-1) and the electrical reactivity of the strong state for crystalline stage is low and on the other hand the Ea is higher (ordinarily 1,200–2,000 J mol-1).

3. Empirical Method Protocol

The exact technique to decide crystalline and shapeless substance in pharmaceutical solids is as per the following: First, an unadulterated medication (100% crystalline) like the medication with obscure substance is analyzed by DEA as a standard. For the unadulterated medication arranged by the pharmaceutical organization the % content before the dissolving temperature is 99.99–100% crystalline and with complete liquefy it is 100% formless in the fluid stage. At that point, DEA re-keep running of the example is performed to dissect the medication with the obscure nebulous/crystalline substance. A consolidated DEA model plot for the % substance of an obscure medication and the unadulterated medication is appeared in the graphical portrayal (Fig. 1) as log ionic conductivity versus temperature. Next, a temperature, Ts, is chosen B30–50 C underneath the dissolving temperature (Tm)

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of the medication from the overlayed DSC bend. At that point, the straight separation (D3) in millimeters of log ionic conductivity on the y-pivot is estimated from 100% strong crystalline line (point X) to the 100% nebulous line (point Z) at the chose temperature Ts. The 100% shapeless or fluid locale is a speculative area and the 100% indistinct line is gotten by extrapolating the fluid district log ionic conductivity of the DEA plot. Next, the direct separation (D2) in millimeters of log ionic conductivity on the y-pivot is estimated from the semicrystalline line (point Y) to the 100% nebulous line (point Z) and (D1) in millimeters from 100% strong crystalline line (point X) to semicrystalline line (point Y) at the temperature Ts are estimated. In the semicrystalline locale, the proportion of shapeless to crystalline substance isn't known.

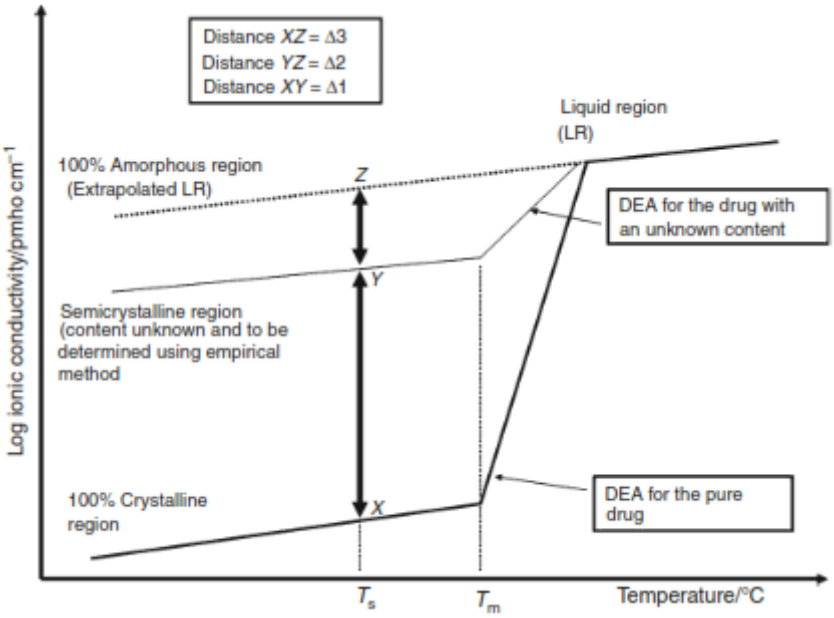

Fig. 1 Graphical representation of DEA empirical method

The linear log conductivity distance in millimeters is a measure from the crystalline phase to the amorphous phase, which is equated to 100%. The Amorphous and crystalline contents can be calculated from the following equations and Fig. 1.

$$\% \text{ Amorphous} = \Delta 1/\Delta 3 \times 100$$

$$\% \text{ Crystalline} = \Delta 2/\Delta 3 \times 100$$

A subsequent strategy was created dependent on an estimation of a DEA enactment vitality Ea (J mol-1) to decide the formless and crystalline substance in medications by DEA. Sharma and Yashonath researched ionic vehicle in an assortment of inorganic formless glasses (solids). They watched a solid connection between's ionic conductivity and actuation vitality. Further, they found that higher conductivity is related with lower actuation energies and lower conductivity is related with higher enactment energies. Their outcomes propose that there is a solid connection between infinitesimal structure of the shapeless strong, ionic conductivity, and actuation vitality.

4. Results and discussions

When Lidocaine is heat cycled through the melt and then cooled back to room temperature. The first DEA run of Lidocaine reveals the crystalline to amorphous phase transition and change in the ionic-dielectric conductivity from B10-2 (pS cm-1) for the crystalline phase and 105 (pS cm-1) for the amorphous phase. Figure 2 shows the DEA surface analysis profile for Lidocaine at 0.5 Hz. Low frequency DEA is confirmed as measurements at the electrode surface, e.g., 0.5 Hz. The Lidocaine (Sigma-Aldrich) sample is initially 99.99% crystalline with very low ionic conductivity for the first run and upon cooling and reheating a huge increase in ionic conductivity was observed. The second and third runs commensurate with an increasing ionic conductivity value of 103 (pS cm-1) (79% amorphous) and 105 (pS cm-1) (91% amorphous) (see Figs. 2, 3). Figure 3 summarizes the % crystalline and % amorphous content in Lidocaine at 0.1, 0.5, and 1.0 Hz by the DEA ‘‘Empirical’’ method. Figure 4 summarizes the % crystalline and % amorphous content in Quetiapine Fumarate (Seroquel) at 0.1, 0.5, and 1.0 Hz by the DEA empirical method. Table 1 shows the list of drugs tested and evaluated for crystalline and amorphous content by the proposed method (Table 1).

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Table 1 Quantification of crystalline and amorphous content in various pharmaceutical APIs by DEA empirical method

Drugs	Average content of second and third DEA runs at 0.1, 0.5, and 1.0 Hz	
	% Crystalline content	% Amorphous content
Sulfapyridine	9	81
Quetiapine Fumarate	10	90
Lidocaine	13	87
Procainamide·HCl	19	81
Lidocaine·HCl	24	76
Indomethacin	26	74
Acetophenetidin	78	22

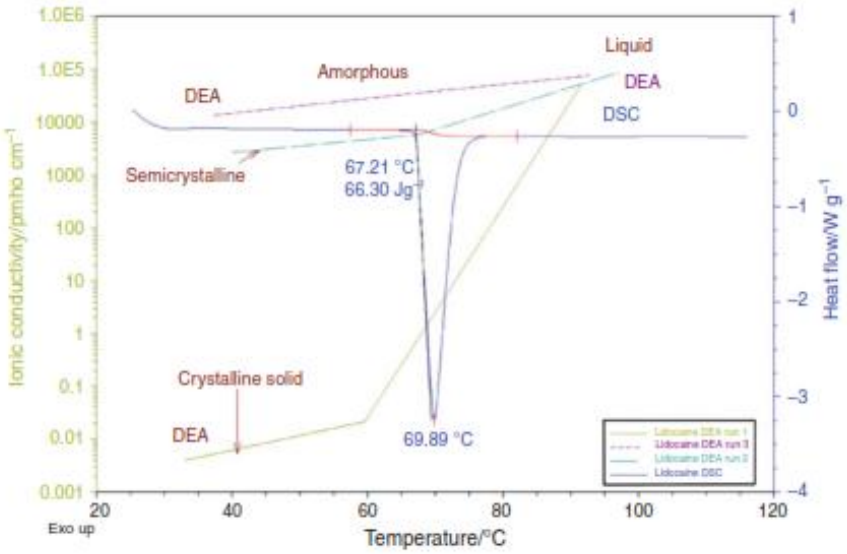

Fig. 2 DEA Surface Analysis of Lidocaine at 0.5 Hz (first, second, third runs); DSC Tm 69.89 C

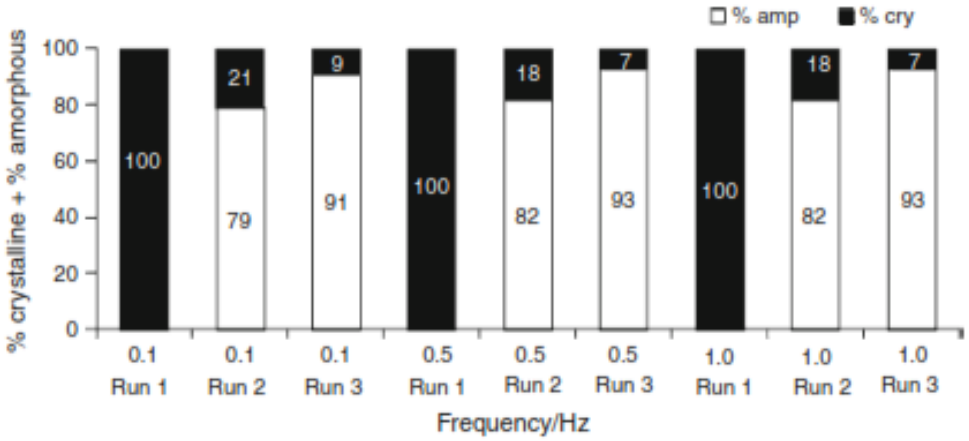

Fig. 3 Determination of % crystalline and % amorphous content versus Frequency/Hz for Lidocaine at 0.1, 0.5, and 1.0 Hz (runs 1–3) by the DEA empirical method. % amp % amorphous content, % cry % crystalline content

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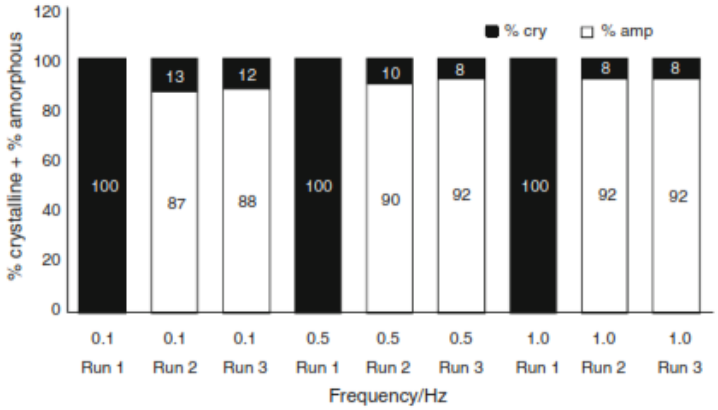

Fig. 4 Determination of % crystalline and % amorphous content versus Frequency/Hz for Quetiapine Fumarate at 0.1, 0.5, and 1.0 Hz (runs 1–3) by the DEA empirical method. % amp % amorphous content, % cry % crystalline content

Our second method to determine crystalline and amorphous content through the measurement of DEA activation energies was tested with several model pharmaceutical APIs. Results for Lidocaine and Acetophenetidin are discussed as follows. Analysis of the Lidocaine by the proposed DEA empirical method yields a supportive interpretation of the activation energy method, i.e., determination of the % crystalline and amorphous content in a drug. Other APIs successfully tested by the activation energy method are Sulfapyridine, Quetiapine Fumarate (Seroquel), ProcainamideHCl, LidocaineHCl, and Indomethacin.

5. Conclusions

The most noticeable end is that we presently have quantitative strategies for deciding the crystalline and nebulous substance of pharmaceutical solids by DEA. We are putting together this end with respect to the realities that the API's appropriated by pharmaceutical organizations are C99.99% unadulterated crystalline solids. When the crystalline state is totally lost during dissolving the material winds up 100% shapeless. Our investigations uncover that six out of the seven medications assessed demonstrated this conduct of complete undefined development. On account of Acetophenetidin, it recrystallized quickly while the others remained dominatingly nebulous. The crystalline and shapeless substance of the medications as dictated by the exact technique was recurrence free. The frequencies contemplated identify with surface examination at 0.1–1.0 Hz. The crystalline and indistinct substance of the medications as controlled by the enactment vitality strategy was recurrence subordinate for one tranquilize, i.e., Acetophenetidin. Accordingly, Acetophenetidin was an exception for these strategies.

References

1. Riga A, Judovits L. Materials characterization by dynamic and modulated thermal analytical techniques. West Conshohocken: ASTM. Special technical publication; 2011.
2. Yu L. Amorphous pharmaceutical solids: preparation, characterization and stabilization. Adv Drug Deliv Rev. 2001;48:27–42.
3. Jo´ja´rt-Laczkovich O, Szabo´-Re´ve´sz P. Amorphization of a crystalline active pharmaceutical ingredient and thermo analytical measurements on this glassy form. J Therm Anal Calorim. 2009. doi:10.1007/s10973-009-0530-5.
4. Cui Y. A material science perspective of pharmaceutical solids. Int J Pharm. 2007;339:3–18.
5. Hancock BC. Disordered drug delivery: destiny, dynamics and the Deborah number. J Pharm Pharmacol. 2002;54:737–46.
6. Hancock BC, Zografi G. Characteristic and significance of the amorphous state in pharmaceutical systems. J Pharm Sci. 1997;86: 1–12.
7. Kere´ J, Sre´ie´ S. Thermal analysis of glassy pharmaceuticals. Thermochim Acta. 1995;248:81–95.
8. Angell CA. The old problems of glass and the glass transition, and the many new twists. Proc Natl Acad Sci USA. 1995;92:6675–82.
9. Byrn S, Pfeiffer R, Ganey M, Hoi berg C, Poochkian G. Pharmaceutical solids: a strategic approach to regulatory consideration. Pharm Res. 1995;12:945–54.
10. Vippagunta Sr, Brittain HG, Grant DJW. Crystalline solids. Adv Drug Deliv Rev. 2001;48:3–26.
11. Venkatesh GM, Barnett ME, Fordjour CO, Galop M. Detection of low levels of the amorphous phase in the crystalline materials by thermally stimulated current spectrometry. Pharm Res. 2001;18: 98–103.
12. Shah B, Kaumanu VK, Bansal AK. Analytical techniques for quantification of amorphous/crystalline phases in pharmaceutical solids. J Pharm Sci. 2006;95:1641–65.

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