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The Scientific Point of View of Pharmaceutical Solids

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ABSTRACT

This review introduces the basic concepts of the material and the principles behind certain common topics in the construction of solid drug formulations. The physiochemical characteristics of micro-organisms are summarized. The general categories, class variations, class modifications, and their relevance to medical development are reviewed. The characteristics and physiological properties of solid phases, including crystalline and amorphous solids, are introduced in conjunction with other relevant chemical phenomena, such as polymorphism, phase transition kinetics, and relaxation. Mesophases, including liquid crystals and condis crystals, were introduced. Potential energy conditions of various categories are highlighted as a key link between the nature of the properties and their pharmacological behavior, and the energy field has been used to increase understanding of these relationships.

INTRODUCTION

In the modern context of drug discovery, it is important to build “drug-like” structures in molecules that are designated to ensure the success of night-time product. However, this policy has been shown to be challenging, especially in many new drug acquisition organizations, where the effectiveness of pharmaceutical procedures and procedures is not yet well established. The challenge stems from a lack of understanding between available teams on basic principles, technologies, and limitations of formula development. As a result, “timely anxiety” is not adequately addressed in the first phase of compound testing. To solve this problem, make-up scientists not only need to provide support for pre-construction, but also have to act as advisors in the findings and ensure that “late time concerns” are well understood and addressed. To help achieve this goal, this article aims to provide academic reviews on strategies to develop drug discovery scientists from a variety of backgrounds.

The development of drug products has long been seen as a field for various sectors. The science of materialism is one of the key branches that continue to provide important information, ideas, and technologies in the construction of science. As an introduction to this broad article, this article should be general, selected, and superficial. The focus is on the development of a solid construction structure. In addition, mesophases have received much attention in the text. This observation, however, highlighted a strong consideration of the properties of the masogenic drug. On the other hand, crystalline chemical systems were not included in this discussion. Although the effects of medicine and piracy techniques were drawn up as key themes, they were influenced by the perspective of practical science and the natural environment below the focus of this paper. Emphasis was placed on the strengths of the various categories encountered in the medical field due to the idea that power directly affects behavioral processes. A strong energy delivery system has been introduced to divide the energy provinces in terms of environmental conditions. While keeping the text straightforward and quality, an effort is made to keep the content in line with current scientific understanding, insights and ideas in this broad area. To give a general and comprehensive view, the reference books emphasize old monographs and review papers.

MOLECULES AND PHASES

Molecules are compounds of atoms linked together by strong chemical bonds, usually bonded bonds. Molecules can usually be divided into two categories according to their size: small molecules referring to molecules with less than 1000 atoms or molecular weight (MW) less than 10,000 Da; while larger molecules (or macromolecules) contain more than 1000 atoms (Wunderlich, 1999). This category is generally correct in most areas. In the case of the agricultural sector, however, it would be appropriate to set a dividing line by 1500 Da. One of the reasons for doing so,

This change varies in cellular molecules between these two layers. In fact, Lipinski pointed out that those molecules with a MW higher than 500 Da may not immediately notice a significant decrease in absorption (Lipinski et al., 1997). At present, the smallest medically important molecules are less than 1500 MW of MW.

Macroscopically, molecules exist in the form of phases. Molecules, whether of the same type or a mixture of different types, can interact with different macroscopic types and different thermodynamic forces. These types of macroscopic, similar and related to the chemical composition and physical condition within the boundary of forms, are called "phases" (Tilly, 2005).

When defining a paragraph, a few points should be kept in mind:

1. Sections must have well-defined boundaries or connectors.
2. Boundaries or crosses should have a negative impact on the objects of the section. This requirement restricts very large components because visible connectors will have a significant impact on “phase” components if the size of the components “decreases” at a sufficiently high rate.
3. Size or scale, where homosexuality is maintained, is important in defining a category. In general, body composition and body size increase as the scale becomes smaller. For example, a solution containing two different types of molecules is visible when viewed on a macroscopic scale (e.g., Micrometer or higher). It is therefore defined as ONE category. However, when the scale is reduced to one molecule, we see molecule A or molecule B, which is clearly different and heterogeneity is evident. Therefore, homogeneity, and thus categories, depends on the scale to be true. Sometimes, when the scale reduces the critical size, the clear definition of the category becomes difficult. In the medical field, for example, the difference between microemulsions and micellar systems containing soluble oil in the core. Both programs contain “droplets” of oil that are distributed over social networks. Micememulson is regarded as a two-phase system, while microcarmons are believed to have only one phase (Attwood, 1994). These layers are sometimes called "microphases" or "nanophases", which have some clarity in their meanings.

Sections are one of the most important topics in medical science. This is for the following reasons:
Stages the maximum presence of a molecule. In active use, molecules are often used in their phases. Therefore, category structures always play a role in applications.
When molecules combine in different ways, e.g. at different distances between molecules or the shape of cells, which produce different phases, usually at different levels of energy. These variations in strength, although often "weak", often have a significant effect on the drug in the combined behavior, including dissolving, bioavailability & stability.
From a different point of view to the same issue, because the cellular interactions that are most important in phase formation are usually much weaker than intramolecular interactions, changes inphase (phase phase) usually do not involve changes in chemical composition / molecule binding. This provides pharmacologists with an important tool for managing phase changes to achieve their goals without damaging the composite structure. In general, it is easy to see that changes in the chemical structure of molecules often lead to phase changes.
Gas, fluid, and solids are the three most common categories. Mesophases, on the other hand, are rare and their function is highly dependent on molecules. Counted as the fourth phase, mesophases consist of liquid crystals, plastic crystals and condis crystals (see Fig. 1). They differ in sharing other properties with both fluid and solids (Wunderlich, 1999). In contrast to the gas and liquid phases, solids and mesophases have many different “subphases,” which will be discussed in more detail later.
Differences between categories can be viewed in a number of ways: intermolecular distance, cell mobility, cellular packing order, and potential energy status. In general, these differences persist: very different distance between molecules; then the cellular movement; the collection of cells is the most subtle. All of this will make a difference in potential power. Therefore, power differences are a natural feature of various categories. This difference is summarized in Fig. 2. Among these differences, cellular movements require extra care. There are three types of "large-amplitude" cellular movements: translation, rotation, and parallel movements, related to "small-amplitude" movements, such as vibrations. The gas and liquid phases exhibit three major amplitude movements, while in crystalline solid solids these movements are absent or “frozen”, leaving only small amplitude movements active. It is important to note that these phase differences, especially the presence or absence of different amplitude movements, are key to classifying categories and understanding their properties. This point will be visited repeatedly throughout the text.
It is interesting to note that “movement” and “lack of order” are often used interchangeably in texts. For example, the movements that take place in other countries contradict the order of certain situations; circular motion lack of directional coordination; and harmonious movement means a lack of harmony. The term "order" refers to certain molecular mechanisms in the cell. It is often true that the loss of certain types / types of order leads to the discovery of the right type / types of cellular movements, and so on. However, these two words do not always change. For example, during amorphous solid delivery, molecules acquire mass amplitude transitions without altering the molecular packing structure (Wunderlich and Grebowicz, 1984). It is similar to the transformation of glass, in which cell loss is lost when no cellular order is found. Here, the differences between the two perspectives should be noted.

CRYSTALS

This apparently simple question can also be rephrased as: Why is there any order in the molecular packing when the molecules are grouped together? Or, what does the order of molecular packing do? Surprisingly, this fundamental question is often overlooked by many authors. It seems that crystalline states and "order" are so ubiquitous around us that an answer to its origin is not necessary. Nevertheless, the reader will find that attempts to answer this question will greatly strengthen our understanding of the concrete steps.

First, a straightforward answer is that crystalline states present low potential energy levels. Therefore, they are thermodynamically more stable than amorphous or other disordered states and there is a tendency that the molecules will pack into crystals.

Then, why is it so? Here the order of molecular packing comes into the picture. By arranging in an orderly manner, molecules can sit more tightly together and pack more efficiently, and thereby reduce specific amounts. This lowers the energy level. Additionally, molecules or atoms often have directional specific intermolecular or intermolecular interactions, such as hydrogen bonds or covalent bonds, that lead to an orderly arrangement of neighboring molecules or atoms. For example, SiO has a silicon–oxygen bond that forms a tetra-hedral short-range order.

Disruption or distortion of this short-range order (also called "local order") increases the potential energy of the system.

A TERRESTRIAL VIEW OF THE CONDENSED PHASES

The energy states of condensed matter, including liquids, crystalline and amorphous solids, can be presented more clearly using the concept of the energy landscape (Stillinger, 1995; Debenedetti and Stillinger, 2001). An example is given in Fig. 4. As mentioned earlier, the potential energy of a phase is determined by several factors, including intermolecular distance and the order of molecular packing. These two factors can be represented by molecular coordination (position, orientation and structure). For example, the intermolecular distance can be expressed as by molecular positions, whereas molecular packing orders only certain types of molecular coordination. An energy scenario arises when the phase potential energy is plotted against the molecular coordinate, as shown in.

First, in the gas phase the intermolecular distance is so large that the interactions between molecules are very weak. As a result, changes in molecular coordination do not affect the potential energy state of the phase. In the liquid state, however, the situation changes slightly. With a shorter intermolecular distance, the intermolecular interaction is stronger and therefore smaller fluctuations in the potential energy state occur when the molecular coordination changes. This can be depicted by Figure 4a and b.

When the temperature is further reduced to below the melting point, the liquid enters the supercooling phase, where the intermolecular distance shortens further and the intermolecular interactions become stronger. This increases the energy fluctuation with molecular coordination because the change in molecular coordination now needs to overcome a stronger barrier and accordingly creates more energy disturbances in the system. At this stage the liquid begins to show structural diversity, where the potential energy at some "preferred" coordinates is lower than at other coordinates (Fig. 4c) (Debenedetti and Stillinger, 2001). It is reasonable to believe that the initial asymmetry is due to some kind of local order, which results from directional intermolecular interactions. This asymmetry becomes apparent as the temperature goes further down and the liquid approaches the glass transition.

The potential energy landscape has gradually advanced from a qualitative concept to a quantitative description of condensed matter. Originating from the projection of Goldstein (Goldstein, 1969), Stillinger and Weber formulated an early theory of the energy landscape (Stillinger and Weber, 1982). The quantitative formulation of the energy landscape is currently under intense research and is progressing rapidly (Sciocortino, 2005). The success of this effort will have fundamental implications in many fields, particularly in amorphous solids and supercooled liquids. Engel and colleagues comment that "... although complex, it is ultimately the only true way of dealing with many-body disorder systems ..." (Engel et al., 2000). This remark certainly applies to crystalline solids as shown in this section. Nevertheless, progress is implied by the available computational power, which is needed to process a large number of molecular coordinates for complex molecules (Debenedetti and Stillinger, 2001). Despite this the compound-dependent energy landscape is not readily available at this point; Its quantitative and complex nature can be appreciated for small organic compounds (Stillinger, 1998).

POLYMORPHISM AND PSEUDO-POLYMORPHISM

Now we must consider why a compound, with only one type of molecule, can organize into different crystalline forms or "polymorphisms". Fig. 5C it is clear that the polymorphs occupy the fewest dips on the energy landscape relative to all other molecular coordinates. This occurs when one type of molecule can occupy multiple coordinates and organize each molecule into a different unit cell (including different dimensions of the same type of unit cell). All of these unit cells can expand continuously in three dimensions, therefore forming many crystalline forms with different energy levels. This is how polymorphism occurs. On the other hand, for some molecules there may only be 1 coordination which allows them to be packed into 1 of the 14 types of unit cells. In these cases, only one crystalline state can be produced. It is easy to understand that the polymorphic phenomenon is compound dependent because the energy landscape is specific to each compound. Detailed structural origins of the polymorphism can be found in the literature (Grant, 1999; Lahani and Grant, 2006).

As the molecular packing orders for the polymorphs are different, the potential energy levels for the polymorphs also differ (see Fig. 5C crystals I and II). A natural question related to this phenomenon is whether a compound can remain stable in various polymorphs under a given condition. Thermodynamically, the answer is no because the polymorph with higher potential energy will sooner or later convert to the one with lower potential energy. Kinematically, however, the conversion rate is variable and can be influenced by many factors. According to Arrhenius law, the conversion rate is determined by

By the magnitude of the activation energy, which is essentially the energy barrier between the two polymorphs.The higher the energy barrier and the lower the storage temperature, the slower the conversion. However, the energy barrier can be affected by a number of factors, such as seeding and impurities (Giron, 2005). An implication of variable polymorphic conversion kinetics is the uncertainty associated with the search for potential polymorphs, especially the thermodynamically most stable polymorphism (McCrone, 1957; Guillory, 1999). Occasionally, the most stable polymorphism may emerge tens of years after the compound was first formed and produced in a metastable crystalline form, which often causes upheaval when it occurs in a marketed drug uct. The reasons are, again, related to the different energy levels of the polymorphisms.

It is now well recognized that polymorphs, due to differences in their potential energy levels, can have a significant effect on the behavior of a compound, e.g., stability, solubility, and bioavailability (Hellebion and McCrone, 1969; Brittain and Grant, 1999). Typically, a metastable polymorph presents higher molecular mobility and therefore poorer chemical stability relative to a more stable polymorph. On the other hand, a metastable polymorph has a higher solubility and therefore its bioavailability is often higher than a more stable polymorph (the difference in solubility is determined by the difference in the energy levels of the polymorph involved and can then be estimated (Pudipeddi) and Serajuddin) , 2005)). These differences in compound behavior are often pharmacologically important. Therefore, conversion from metastable to more stable polymorphs can affect the performance of a pharmaceutical product, sometimes resulting in the failure of a marketed product. To control exposure, the thermodynamically most stable crystalline form is always preferred in current pharmaceutical practice. Sometimes, the most stable polymorphism may not provide sufficient bioavailability, whereas a metastable form can. In these circumstances, metastable polymorphs may be attempted, often tentatively, to support some non-clinical or clinical studies. However, it has often been found that once more stable polymorphs have been generated the consistent production

of metastable polymorphs is difficult, if not impossible, which presents a major challenge for supply chain management. Therefore, avoiding using metastable polymorphs appears to be the current industrial trend. In any case, the discovery and evaluation of polymorphisms and their thermodynamic relationships are important activities in the selection of suitable polymorphisms for drug development. Unfortunately, there is always a risk that the "most stable polymorph ever found" may become a metastable and a more stable polymorph may emerge in the future, due to the variable kinetics of polymorph transformation. Therefore, in addition to polymorph screening, frequent monitoring of crystalline forms is important in drug development.

Similar to polymorphs, the occurrence of hydrates, solvents and co-crystals can also influence the drug candidate's development strategy. Nevertheless, the situation may be more complicated with hydrates or solvents. Before going into more detail, it should be noted that although hydrates, solvates, and co-crystals are formed from two compounds, which differ by polymorphisms, they are also specific physical phases that an API can exist in. In. Thus, they are called "pseudopolymorphs", in a sense to show their similarity with "real" polymorphs (Bechtloff et al., 2001). These steps are often encountered in the pharmaceutical development process. For example, water and moisture are often involved in the processing and storage of medicinal substances and pharmaceutical products, which can lead to the formation of hydrates. Solvents are commonly used in the manufacture of pharmaceutical substances, during which solvents can be produced.

AMORPHOUS STATE

The amorphous phase, also called glass, is another commonly encountered solid subphase. Despite that amorphous materials have many important applications and a lot of in-depth studies have been devoted to this field in the last century, the structural explanation of amorphous materials is still incomplete. As described earlier, the molecular arrangement of the amorphous state lacks long-range order, which is a unique feature of crystals. However, short-range ordering has been found to be widely present in inorganic amorphous materials. SiO2 is again converted into an. to use as, For example, it was found in amorphous SiO to have tetrahedral local order conserved (see Figure 3A), but the long-range diffusion of the order is missing (Ossi, 2003). Obtained from studying inorganic glasses such as SiO2, this conclusion has been extrapolated to other amorphous materials, such as organic small molecules, without vigorous experimental evidence. In fact, up to this point most structural studies in the amorphous state have mainly focused on inorganic materials because of its simplicity. The lack of suitable experimental techniques and the complexity of data analysis for other amorphous systems must account for this unsatisfactory situation. When discussing the existence of a local arrangement in organic small molecule glasses, it should be noted that this is actually a projection, although with proper premise.

The discussion on the amorphous state can be organized by following the energy scenario. In fact, an early theory of the energy landscape was proposed to describe the glass and glass transition (Stillinger and Weber, 1982; Stillinger, 1995). This approach will be employed below.

HIGH POTENTIAL ENERGY

Amorphous solids present many special and intriguing properties that have found various important applications. One of the most fundamental properties of an amorphous solid is its high potential energy state relative to crystalline forms. It is now clear that amorphous forms, due to their low packing efficiency and lack of long-range ordering, present higher potential energies than their crystalline counterparts (Yu, 2001). What does higher energy state mean to scientists? Similar to metastable polymorphs, it can affect the properties of pharmaceutical products in several aspects: physical and chemical stability, solubility, and bioavailability (Hancock and Zeography, 1997).

First, higher potential energy means physical instability and potential conversion to the thermodynamically more stable crystalline form can occur over time. Again, the conversion rate is decided by kinetics. If the kinetics is sufficiently slow relative to the pharmaceutically important time frame, amorphous states can still be used in pharmaceutical products (Dannonfelser et al., 2004).

Second, because of their high molecular mobility, amorphous forms often exhibit strong chemical reactivity and thus show rapid chemical degradation rates. More specifically, the chemical degradation rate is dependent on the energy state of the glass and the scale of the molecular movement that is specifically involved in the degradation reaction. As mentioned earlier, some types of large-amplitude molecular movement in amorphous states are still active under a given temperature, but at a slower rate. If these active modes of movement are involved in particle-

Chemical degradation of the compound, the degradation rate is certainly faster than in the crystalline state (Jiang and Anderson, 2004).

Finally, amorphous forms often present high solubility. This provides a great tool for scientists to increase the bioavailability for those sparse water-soluble compounds. In fact, recently amorphous forms have attracted increasing interest in the field mainly because of this valuable property. The solubility enhancement of amorphous forms over crystalline states depends on the potential energy difference between these physical states. In a study involving a limited number of model compounds, it was estimated that 10–1600-fold of solubility enhancement could be achieved by applying amorphous glasses (Hancock and Park, 2000). Of course, the trade-off for increasing solubility is chemical stability and the risk of possible conversion of amorphous forms into crystalline states. Therefore, the benefits and risks of this strategy need to be carefully evaluated during the development process.

MESOPHASES

Mesophases are intermediate states between a crystalline solid and a liquid. The word "mesophage" is derived from the Greek word "meso", which means "in the middle". Recall properties of liquids and crystalline solids: Molecules in liquids exhibit all large-dimension mobility, including translational, rotational, and conformational mobility, whereas mobility in crystalline solids is almost absent. If the restriction on molecular mobility

Crystalline solids are partially raised, intermediate states arise. Based on the types of molecular dynamics existing, these states can be classified into liquid crystals (with positional and, if applicable, conformational mobility), plastic crystals (with orientational mobility), and condice crystals (with conformational mobility). could. Among them, liquid crystals and plastic crystals have long been well-known mesophases (Kleiman and Lavrentovich,

2003; Sherwood, 1979), while conditionals are relatively new. The term "condis crystal" was coined in 1984 from a contraction of "correctly disordered crystal" (Wunderlich and Grabowicz, 1984). However, the existence and properties of conformationally disordered crystals have been recognized and studied since much earlier times (Smith, 1975). Due to the fact that most disordered crystals are observed in partially crystalline polymers, it has long been viewed as part of a polymeric crystal rather than a type of mesophase (Wunderlich, 1989). Nevertheless, Condis crystals have also been found in small organic molecules (Wunderlich and Grabowicz, 1984). Although rarely seen in publications, condis crystals have appeared among developmental drug candidates to the knowledge of the authors. However, they were often mistakenly regarded as crystalline polymorphs with incompleteness or weak lattice energies. For the purpose of this work, the mesophase concept of Kandis crystals has been adopted to emphasize their intermediate nature and to differentiate them from crystalline polymorphisms.

To better understand the general properties of these three mesophases, it is useful to compare their thermodynamic states with those of isotropic liquids and crystalline solids. Comparisons can be made between these phases by determining the phase transition entropy (Wunderlich and Grabowicz, 1984). It was found that the liquid crystals are quite close to the isotropic liquid phase in their free energy states, indicating that the orientational order in the liquid crystal is quite incomplete apart from the absence of positional and conformational order. Condis crystals, in contrast, are quite close to crystalline solids, although the difference in their energy states varies with the number of structurally flexible bonds in the molecules. In fact, the properties of Condis crystals, which maintain positional and orientational order, deviate only slightly from those of perfectly arranged crystalline solids. This is the major reason why Condis crystals are often mistakenly treated as crystalline polymorphs. Finally, despite the plastic crystals being between these two mesophases, they exhibit a higher positional order. In short, liquid crystals, plastic crystals and condys crystals are becoming increasingly more solid (Wunderlich, 1989). Another important characteristic of mesophases is their intermediate mechanical properties between those of liquid and solid, which are often overlooked by many. From a mechanical point of view, an "ideal" liquid is completely plastic, meaning that the deformation of an "ideal" liquid under tension is completely unattainable in itself once the tension is withdrawn. In contrast, an "ideal" solid is perfectly elastic; This means that its deformation under tension is fully recoverable by elasticity once the tension is withdrawn. Mesophases are usually either viscous liquids or semi-solids or soft solids whose deformation is partially and/or slowly recoverable. Therefore the device-

The typical behavior of mesophases is between a typical liquid and a solid. This property is what differentiates mesophases from amorphous solids. The latter is also an intermediate state structurally and energetically between a liquid and a crystalline solid. However, amorphous glass behaves mechanically like a crystalline solid, whereas typical mesophases are either viscous liquids or soft solids. Of course, structurally the mesophase presents a certain degree of long-range ordering, which is absent in amorphous solids (Dearing, 2003).

The intermediate mechanical strength of the mesophase results from the physical nature of the material. First, mesophases are formed by organic molecules bound by weak intermolecular interactions (Kleiman and Lavrentovich, 2003). Additionally, the phases are partially arranged and thus no strong crystalline lattice energies are present. This physical nature leads to the phase transition temperature of the mesophase which is often close to room temperature and relatively small transition enthalpies are often observed. For scientists low-temperature phase transitions often mean stability or quality control issues that require special care.

The ability to form different mesophases largely stems from the structure and geometry of the molecules. Molecules in condition crystals have flexible structures and do not suffer structural changes with high activation energies. Liquid crystals always have a rigid rod- or disc-like core molecular structure, which causes a high activation energy for rotational rearrangement and thus maintains some degree of orientation order. Plastic crystals, in contrast, are more spherical in their molecular shape, so that the energy barrier for recrystallization is lower. As a result, molecules can move freely within the crystalline lattice at certain temperatures, indicating that the orientation order is lost, while the crystalline structure remains intact. Roun d shape. Although the application of LC systems in areas has a long history, most of the attention has been focused on LC drug delivery systems rather than APIs. Historically, surfactants, cholesterol derivatives, phospholipids and several lipid families have been common LC formers applied in various liquid delivery systems. Recently, some cellulose derivatives, which are commonly used in solid dosage forms, were also found to exhibit LC phases (Ambrosino and Sixsou, 1989; Sixsou, 1999). These excipients include hydroxypropylcellulose (HPC), ethyl-cellulose (EC), and cellulose acetate (EA). Over the past several years, the APIs that make up LC began to attract attention in the pharmaceutical sector (Bunges and Reds, 2005; Stevenson et al., 2005). Although the interest of scientists in LC systems is increasing, it appears that the development strategy for this class of APIs has not been fully addressed.

KANDIS CRYSTAL

The molecule or part of the molecules in Condis crystals is structurally flexible. Many chemical structures can have conformational isomers. The formation of conditional crystals depends on the magnitude of the activation energy involved in the conformational changes. A lower activation energy leads to a higher conformational freedom and hence a higher probability of Condis crystal formation. For example, linear aliphatic chains with smaller substituent groups encounter less resistance in conformational motion about the chain axis. Some polymers, such as polyethylene and polytetrafluoroethylene, are characterized by this structure and they exhibit Condis crystal phases at elevated temperatures (Wunderlich, 2006; Wunderlich, 1999). Many LC formers, especially lyotropic LCs, present condys crystal phases at low temperatures when they turn into solids or plastic solids. These molecules, such as soaps and surfactants, often contain flexible long-chain aliphatic groups. Indeed, flexible chains are the most common structures that drive the formation of Condis crystals, although other structural features, such as boat/chair ring conformations, have also been reported (Glaser et al., 1990; Wunderlich and Grabowicz, 1984).).

Condis crystals are particularly more noticeable in the regions because they are closer to crystalline solids in general. This characteristic, as discussed earlier, often causest to be confused with Condis crystal crystalline polymorphisms. The challenges of condis crystals in solid fabrication development mainly result from their low crystallinity and weak mechanical strength. Compounds that show the Kandis crystal phase, when crystallized, often exhibit low or incomplete crystallinity due to the conformational flexibility of their molecules. When water or heat is involved in the processes, some of the compounds may be released into the amorphous state upon recrystallization. In addition, condis crystals are easy to deform mechanically, which is often accompanied by some degree of amorphousness. Uncontrolled amorphization raises concerns for the quality control of pharmaceutical products.

On many occasions this can mean that the development of tablet formulations is nearly impossible. In some companies, this actually leads to the termination of a delivery candidate. Therefore, it is important to identify Condis crystals and separate them from fully ordered crystalline polymorphs. This can be achieved in most cases through conventional thermal analysis (Wunderlich, 1989). Additionally, mechanical stress should be investigated before a compound is selected for potential crystalline form transformation and growth on water.

CONCLUSION

There is a growing interest in formulation strategies and ideas among drug discovery scientists. The purpose of this paper is to provide some background and insight into this area by addressing the physical nature of solid systems. It is clear that this text is by no means complete. For example, liquid and colloidal systems are commonly applied in early drug discovery support, demanding detailed discussion. Due to the size limit, this paper is unable to address these important topics. Readers are encouraged to refer to other literature on interested subjects.

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