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A Comprehensive Mini Review on Co-Crystallization Process

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Authors' contributions

This work was carried out in collaboration among all authors. Authors AMD and RA designed the study and wrote the first draft of the manuscript. Authors FA and BKD managed the analyses of the study and update the manuscript. Authors RA and SS managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Co-crystal chemistry has recently attracted supramolecular scientists. Co-crystals are comprising of hydrogen bonding assembly between different molecules. Many issues related to the performance characteristics of an active pharmaceutical ingredient (API) can be resolved using the co-crystallization approach. A proper understanding of the crystal structure of an API is required for the successful formation of co-crystals with the selected co-former. Co-crystal chemistry has recently attracted scientists from the super molecules. Co crystals consist of the assembly of hydrogen bonds between various molecules. Many problems related to the performance characteristics of an active pharmaceutical ingredient (API) can be solved using the method of co-crystallization. Co-Crystals offer an alternate pathway where any API, paying little mind to be acidic, essential, or ionizable gatherings, might be co-gem. This aspect also helps to complement existing methods by reintroducing molecules with limited pharmaceutical profiles based on their non-ionizable functional groups.

Keywords: Co-crystals; supramolecular complexes; nonionizable; functional groups; properties; production & characterization; application of co-crystals.

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1. INTRODUCTION

The most common state of delivery of the dosage form is solid, such as tablets, capsules, etc [1-2]. Various other states exist that allow the delivery of the API faster than the solid-state. But this state provides the most convenient, compact, and stable API to store. Thus, the understanding and control of solid-state chemistry become a vital part of drug development [3-5]. The API cannot be formulated many times in its performance due to a variety of instability issues.

Co-crystals are solids that are crystalline single-phase materials composed of two or more different molecular and ionic compounds held by non-covalent interactions in a stoichiometric ratio that are neither solvents nor pure salts [6-8]. Presently, the previous can be some other excipient or API that decreases the portion and the reactions when given in mix [9]. Even if the API changes the same, the previous will likewise improve the pharmaceutical properties (synthetic soundness, bioavailability, dissolvability, softening point, dampness take-up, disintegration, and so on).

2. HISTORY

The first co-crystal reported, quinhydrone, was studied by Friedrich Wöhler in 1844 [10]. Quinhydrone is a quinone and hydroquinone co-crystal (archaically referred to as quinol). He found that this material consisted of a 1:1 molar combination of the components. Several groups analyzed quinhydrone over the next decade, and several related co-crystals were made from halogenated quinines [11]. Numerous co-crystals found in the late 1800s and mid-1900s were accounted for in Organische Molekulverbinducngen, published by Paul Pfeiffer in 1922 [12]. This book divided co-crystals into two categories: inorganic: organic components and organic components.

Co-crystals continued to be discovered throughout the 1900s. Some have been found by some coincidence and others by screening strategies. Information on the intermolecular connections and their consequences for precious stone pressing permitted the building of co-crystals with the ideal physical and compound properties [13]. In the most recent decade, there has been an expanded enthusiasm for co-crystal research, principally because of utilizations in the pharmaceutical business.

3. PROPERTIES

The properties of a co crystal always depend on the co-former based on formulation [14]. The types of intermolecular interactions are usually occur during co crystallization process depends on chemical properties of the co former [15]. This co crystallization process to improve the physicochemical properties of the drugs. The salt formation during co crystallization are found in micronization and amorphization [16]. Segments connect through non-covalent collaborations, for example, hydrogen holding, particle associations, van der Waals communications, and PAR-cooperation's [17]. These interactions lead to co-crystal lattice energy, which is generally more stable than the crystal structures of the individual components. Intermolecular collaborations and coming about precious stone structures can produce physical and synthetic properties that vary from the features of the different parts [18]. These properties include melting point, solubility, chemical stability, and mechanical properties. Some co-crystals have been observed to exist as polymorphs, which may exhibit different physical properties depending on the shape of the crystal [6].

The phase diagrams determined by the "contact method" of thermal microscopy are valuable for the detection of co-crystals [19]. The development of these stage charts is made conceivable by an adjustment in the softening point in the wake of co-crystallizing. Two translucent substances are kept on either side of the magnifying instrument slide and are successively liquefied and re-cemented [20]. This process creates a thin film of each substance in the middle of a contact zone. The melting point phase diagram may be constructed by slow heating of the slide under a microscope and by observing the melting points of the various portions of the slide [21].

4. PRODUCTION AND CHARACTERIZATION

4.1 Production

There are numerous engineered techniques accessible to plan co-crystals. Nonetheless, it might be hard to plan single co-crystals for X-beam diffraction, as it is known to take as long as a half year to set up these materials [22].

Co-crystals are ordinarily produced by moderate dissipation of the arrangements of the two segments. This methodology has been effective with atoms of correlative hydrogen holding properties, in which case co-crystallization is probably going to be thermodynamically liked [23]. There are many other methods for producing co-crystals. Crystallizing with a molar excess of one co-crystal former may produce a co-crystal due to a decrease in the solubility of that one component [24]. Another method used to synthesize co-crystals is to conduct crystallization in a slurry. As with any crystallization, consideration of solvents is important [25]. In addition, phase considerations may be used by changing the solvent. The role of solvent in the nucleation of co-crystals remains poorly understood but critical in order to obtain a co-crystal solution [26].

Cooling the liquid blend of co-crystal exfoliants regularly takes into account co-crystals [27]. Seeding can be useful. Another methodology that adventurous stage change is sublimation, frequently shaped by hydrates [28].

Grinding, both neat and liquid-assisted, is used for the production of co-crystal, e.g., by the use of mortar and pestle, the use of a ball mill, or the use of a vibratory mill. A little or substoichiometric measure of fluid (dissolvable) is added to the crushing blend in the fluid helped to granulate or working procedure. This technique was created with the end goal of expanding the pace of co-gem development, however it has points of interest over flawless pounding, for example, expanded yield, capacity to control polymorphic creation, improved product crystallinity, and applies to a significantly larger range of co-crystal molds.

Supercritical fluids (SCFs) are used as a medium for growing co-crystals. Crystal growth is achieved through the use of different supercritical fluid properties due to the unique properties of SCFs: supercritical CO2 solvent power, anti-solvent effect, and enhancement of atomization.

4.2 Crystallization Process [29-30]

- Solute leaves the solution to be in the company's crystalline lattice.
- Thermodynamics and kinetics:

  - SLE data.
  - Rate of crystallization mechanisms expressed mainly as supersaturation functions (driving force).
  - Mechanisms for the generation of supersaturation.
  - Implications of heat and mass transfer during kinetic scale-up process.
  - Other Balance Data.

4.3 Characterization

Co-precious stones can be described in a wide assortment of ways. Powder X-Ray diffraction ends up being the most generally utilized strategy for portraying co-gems. It is easy to see that a unique compound is formed and if it could possibly be co-crystal or not because each compound has its own distinct powder diffractogram [31]. Single-precious stone X-beam diffraction may demonstrate troublesome on some co-crystals, particularly those shaped by pounding, as this technique as a general rule produces powders. However, these forms can often be formed by other methods in order to provide for single crystals. Apart from common spectroscopic methods such as FT-IR and Raman spectroscopy, solid-state NMR spectroscopy allows the differentiation of chiral and racemic co-crystals of similar structures [32].

Other physical characterization methods may be used. Thermogravimetric analysis (TGA) and differential calorimetric scanning (DSC) are two commonly used methods for the determination of melting points, phase transitions, and enthalpic factors that can be compared to each individual co-crystal form [33].

5. APPLICATIONS

Co-crystal building is applicable to the creation of vitality materials, pharmaceuticals, and different mixes. Of these, the most generally contemplated and utilized applications are the improvement of medications and, all the more explicitly, the arrangement, plan, and execution of dynamic pharmaceutical fixings (APIs) [34]. Changing the structure and creation of the API may significantly affect the bioavailability of the drug. Co-crystal engineering takes advantage of the specific properties of each component to make the most positive conditions for solvency that could, at last, upgrade the bioavailability of the medication [35]. The principle thought is to create prevalent physical-substance properties of the API while keeping up the steady properties of the medication atom itself. Co-crystal structures have also become a staple for drug discovery. Structure-based virtual screening methods, such

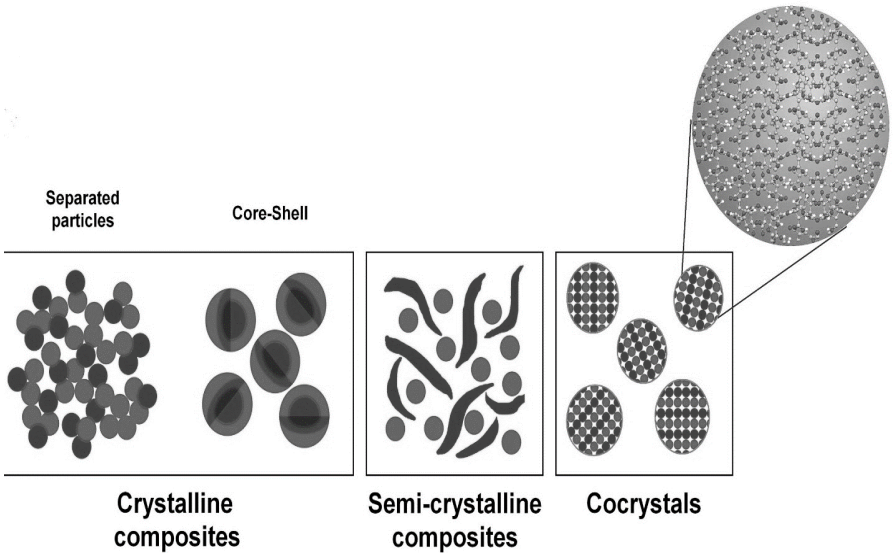

Fig. 1. *Co -crystallization* process

as docking, use co-crystal structures of known proteins or receptors to elucidate new ligand-receptor bindings [36].

- Pharmaceuticals co-crystal may improve certain physical and chemical properties (e.g., stability, water-solubility, dissolution rate, bioavailability) of the active pharmaceutical ingredient (API) without compromising its action [6,37].

The co-crystallization process can be used to perform difficult separations e.g., Racemic mixtures, Recuperation of vanillin.

6. PHARMACEUTICAL

In the field of pharmaceuticals, co-crystal engineering has become so important that a particular subdivision of multi-component co-crystals has been given the term pharmaceutical co-crystals to refer to a solid co-crystal ex-segment and anatomic or ionic API (dynamic pharmaceutical ingredient) [38]. The objective for pharmaceutical co-crystals is to have properties that vary from those expected for pure APIs without the creation and rupture of covalent bonds [7,39]. Sulfonamides are among the first pharmaco-crystals reported [40].

A case in point is the drug sulfathiazole, a common oral and topical antimicrobial with more than a hundred different solvent [41] s. It is, therefore, important in the pharmaceutical field to screen for every polymorphic form of co-crystal before it is considered to be a sensible improvement to the current API. Pharmaceutical co-crystal development can likewise be driven by numerous API functional groups, which introduce the possibility of binary, ternary, and higher-ordered co-crystal forms [42].

Multiple drugs combination (MDC) co-crystallization has become a popular new drug development strategy [43]. Its abilities to enhance the treatment effect and decreases the adverse effects of drugs [44]. Multidrug co-crystallization is the recent technique for the design of solid APIs, the use of this technique may improve co-crystals potential applications of new drugs combination [45-46]. This process of MDC improved properties of the combination drugs and improve therapeutics efficacy for new drug development [47]. Hence, the idea of developing a multiple-drug co-crystal is reflected in recent applications [48-49]. The multidrug co-crystals are consider as solid crystalline supramolecular complexes that are highly therapeutically effective components in management of chronic disease. This definition was reconstructed based on FDA guidelines according to which co-crystals are dissociable multi-component solid crystalline supramolecular complexes composed of two or more components within the same crystal lattice [47]. The multidrug co-crystals implement the patent eligibility criteria such as non-obviousness, novelty, and utility for pharmaceutical development [50].

7. CONCLUSION

Pharmaceuticals are the pillar of the healthcare sector. It, in this way, presents a significant test in planning another sort of conveyance framework or modifying the API structure to upgrade or improve the qualities that block its adequacy. Thus, in the event that of co-crystallization, it is another technique that can be utilized to defeat different physical, concoction, or physiological disadvantages particle an API. On account of the plan angle, co-crystallization offers another zone for the advancement of another strategy for readiness, the portrayal of the API. It can, therefore, act as an opportunity for industries wishing to claim the intellectual property. New techniques for the screening of these APIs are another challenging area.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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