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A Method to Enhance Solubility and Tableting Properties by Particle Size Enlargement-Crystallo-Co-Agglomeration

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Abstract

Crystallo-co-agglomeration is a novel particle design technique, to overcome the limitations of spherical crystallization. The process of Crystallo-co-agglomeration involves crystallization followed by simultaneous agglomeration of the drug with the aid of either a good solvent or a bridging liquid and a bad solvent. The agglomeration is performed using bridging liquid. In the field of powder technology various attempts has been made to design primary and secondary particles of pharmaceutical substances for various applications, such as improvement in solubility of drugs, obtaining suitable polymorph, improvement in micromeritics and compression properties, and modification of bioavailability.

Key words: Crystallo-co-agglomeration, micromeritics, bioavailability

Introduction

In the ground of powder technology attempts are undertaken to design primary and secondary particles of pharmaceutical substances for various applications, such as improvement in solubility, obtaining suitable polymorph, improvement in micromeritics and compression properties, and modification of bioavailability. The method of Spherical crystallization is a nonconventional method of particle-size enlargement that involves crystallization and agglomeration using bridging liquid. Different methods have been reported to achieve supersaturation during spherical crystallization. The method of Spherical crystallization used mainly to obtain directly compressible agglomerates of a single, water-insoluble large-dose drug, and rarely in combination with diluents. There are very few expositions regarding application of Spherical crystallization for obtaining agglomerates of more than 1 drug. The applications of this method to obtain directly compressible agglomerates without diluents are restricted to water insoluble large-dose drugs. Most of the excipients, such as diluents and disintegrating agents, are hydrophilic in nature; hence, incorporation of these excipients in the agglomerates formed using organic bridging liquid is difficult. Spherical crystallization could not be applied to obtain agglomerates of low-dose or poorly compressible materials which is its major limitation,

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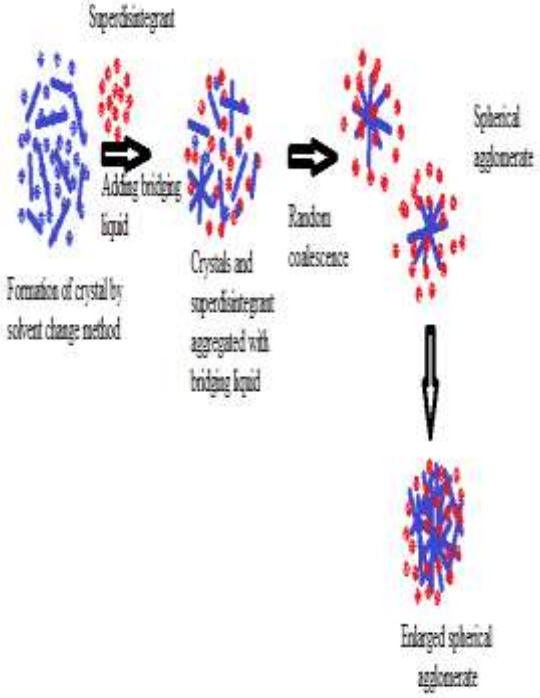
Advantages of Crystallo-Co-Agglomeration

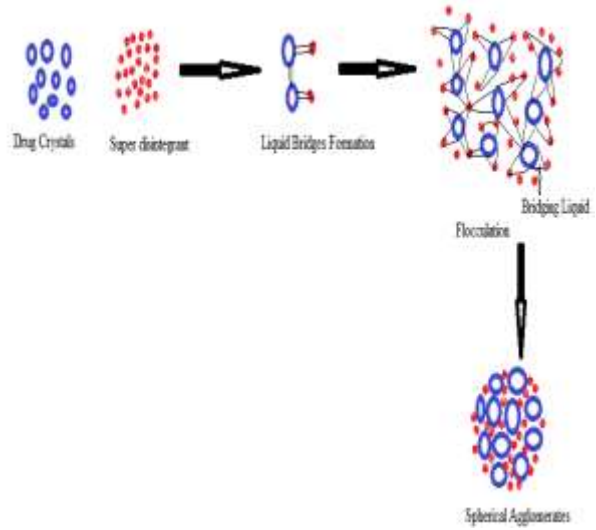
Mechanism of CCA Formation

The mechanism of crystallo-co-agglomeration is simply the crystallization and agglomeration of drug with excipients using bridging liquid.



Mechanism of Bridging Liquid

Bridging liquids forms the physical bridges between the drug and excipients to form compact entity



Method of Preparation of agglomerates

Characterization of Crystallo-co-agglomeration

1. % yield
2. Entrapment efficiency
3. Amount of disintegrant
4. DSC
5. XRD
6. Micromeritic properties
7. Particle size
8. Angle of repose

9. Carr's index
10. Hausner's ratio
11. Tapped and Bulk density
12. Solubility studies

Conclusion

Crystallo-co-agglomeration technique has been developed to overcome the limitations of spherical crystallization and used for size enlargement of all, low dose, high dose, poorly compressible drugs and combination of drug with or without diluents. It involves combination of crystallization and agglomeration using bridging liquid and crystallization medium. This technique is simple carried out in a single step and more advantageous due to less number of unit operations and economic in terms of processing cost.

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