Analysis of Growth and Development of Liquid Crystals in Pharma Ceutical Applications

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ABSTRACT
Our society's healthcare system is in desperate need of reform. Work on the development of novel pharmaceuticals requires the collaboration of scientists from both industry and academia. Oral dose forms containing crystalline solids of the active ingredient are the chosen mode of administration for the majority of medications. Crystallization is consequently essential in medication development, as it produces crystalline active pharmacological ingredients (API). The creation of a process relies heavily on an understanding of the impact of key process parameters on the final product's qualities. The development of crystallisation processes at the laboratory scale can currently be supported by a number of technologies. There are numerous technologies that can be employed to construct pharmaceutical crystallisation procedures. A method is presented for organising, designing, and carrying out laboratory-scale crystallisation studies in a reliable manner. This approach enables precise control of the essential crystal qualities that influence the new drug's pharmacokinetics and bioavailability, among other things. A focus on laboratory research to aid in the creation of new pharmaceuticals is emphasised throughout the piece.

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1. INTRODUCTION

It is a type of matter that exists between the crystalline and liquid phases, with special traits such as the loss of the anisotropic molecule positional order in a state of matter specific fashion. Since they have so many outstanding and useful optical and physical features, liquid crystals (LCs) are essential electro-optical materials for modern technology. LCs (liquid crystal displays) are commonly utilised in television screens, display media, and personal computers. For the most part, these LCs can be made using several precursors, such as a hydrophobic core, a flexible chain, or a combination of the two. A variety of organic cell structures, such as cell layers, also contain amphiphilic phospholipids[1].

These interactions between LCs and biological cell structures are possible because of LCs or their predecessors, liquid crystal related compounds (LCRCs). There is a growing interest in discovering the natural and pharmaceutical effects of these crystal compounds. Recently, the

use of LCs in biological sensing and drug administration has garnered a lot of interest for usage in analgesics, anticancer, liver disease, anti-asthmatic, and nanoparticle formulations[2]. Anisotropic molecules' birefringent characteristics enabled these LCs to function via biosensor activity. This birefringent orientation allows for a change in the LC's optical appearance during the course of the biological event or in the presence of Surprisingly, the assembly of phospholipids between the nematic LC 4-Cyano-4′-pentylbiphenyl (5CB) and aqueous phase is critical in transforming nematic liquid crystals from planar to homeotropic.

When seen under a microscope (crossed polarizers) known as a polarised optical microscope, the optical texture of 5CB can be changed from dark to bright (POM). Aside from this, LCs have been used to monitor real-time enzymatic activities, identify immobilised peptides and proteins, as well as identify the orientation of immobilised proteins. LCs, particularly thermotropic LCs, have also been shown to play a role in stem cell research, with embryonic stem cells and embryogenesis benefiting from their use. Neurodegenerative disorders such as Alzheimer's disease, Gaucher's disease (lysosomal storage disorder), steatohepatitis mouse models, and atherosclerosis have indicated that LCs play an important role in the rearrangement of the extracellular matrix and growth and differentiation. The "dependent features of LCs" were also employed to distinguish between lipid bilayer-enclosed and non-enveloped viruses in the diagnosis of sepsis, in addition to the previous applications. LC-based bio-sensing has the potential to play a role in diagnostics and clinical applications because of its fast, label-free, and low-cost capabilities. However, to the best of our knowledge, no reviews have been done on the significance of liquid crystals in cancer biology and biomarkers, despite the fact that many researchers have used them. Progress is being made rapidly in the field of LCs, despite a lack of discussion on their use in the detection of cancer biomarkers.[3]

2. MATERIALS AND METHOD

- **Materials**

The information needed to create a reliable crystallisation process can be gathered and evaluated using a methodical approach. For crystallisation process development, a seven-step technique has been devised, which includes planning, screening, optimising, and testing

- **Preparation stage**

Defining the aims of the experiments and the context in which they will be carried out is an important part of the planning process. Identifying the crystal qualities that have a significant impact on the final drug's attributes and performance is a priority in the early stages of planning. Several crystal qualities are linked to the final performance of a pharmaceutical product, including crystal size, morphology, polymorphism, and distribution of crystal size. For example, the quick disintegration and resulting bioavailability of tiny crystals makes them useful in some instances. To avoid manufacturing issues in downstream processes like

filtering and drying, narrow particle size distributions are typically favoured. The clarity of the crystals may also have an impact on the stability of the medication.

- **Pre-Screening**

Initial small-scale tests are carried out to identify prospects for further research as part of screening. Initial screening may be carried out using high-throughput technologies. In a workstation, high-throughput screens make it possible to efficiently run a large number of experiments at small scales. Solvent screening and polymorph screening are two of the most common screening techniques used in the development of crystallisation processes. Solubility and metastable zone width curves, as well as kinetic characteristics of nucleation and growth rate parameters, are used to evaluate the most promising candidates in the solvent screening process, which includes additional experiments.

- **Optimization Stage**

The pharmaceutical industry benefits greatly from the identification and characterization of polymorphs. Time and resources can be wasted if an improved polymorphic form is discovered too late in the game. Polymorphic transformation investigations are carried out to determine the pace at which metastable to stable forms are transformed.

- **Validation Stage**

A series of additional experiments will be done to ensure that the "optimal process conditions" are achieving the desired crystal characteristics after evaluating the effects of various factors. At this point, the experiments' initial goals have been met, and the potential for scaling up has been assessed. For future advancement, this process is documented with all of the necessary data that was gathered at lab scale.

3. RESULTS

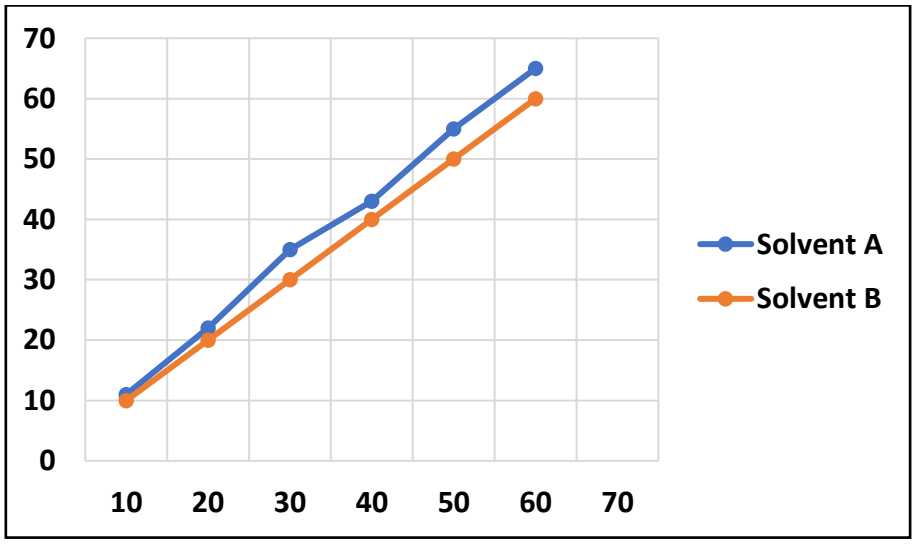

Fig 1 Distinct solvents have different solubility curves.

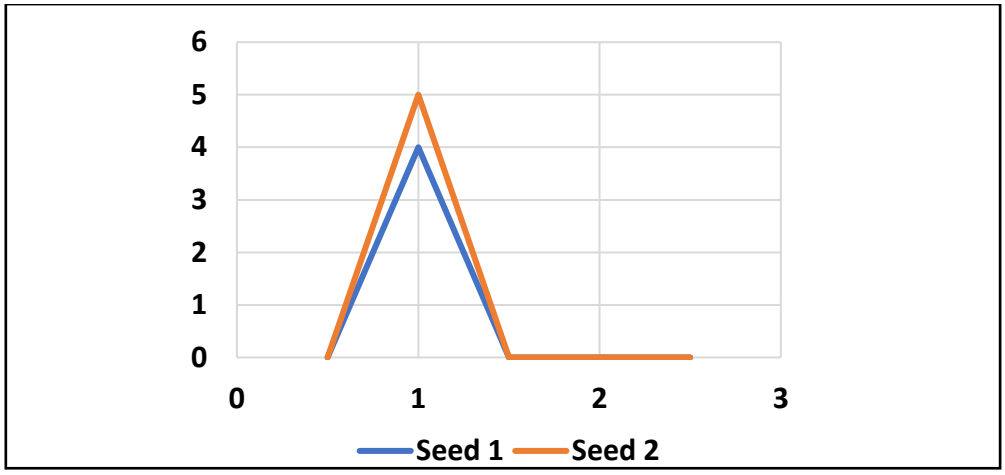

Fig 2: The effect of seed size on polymorphic transformation rates

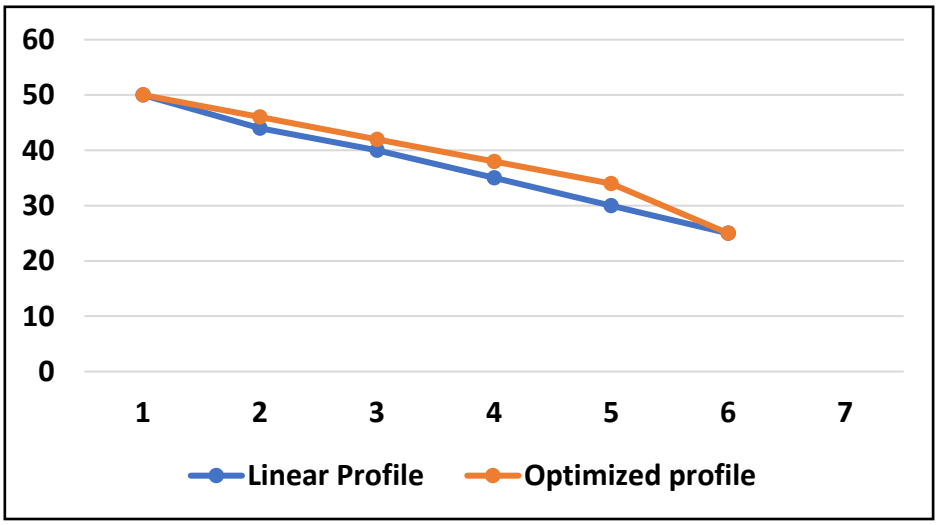

Fig 3.The effect of a cooling profile on particle size distribution

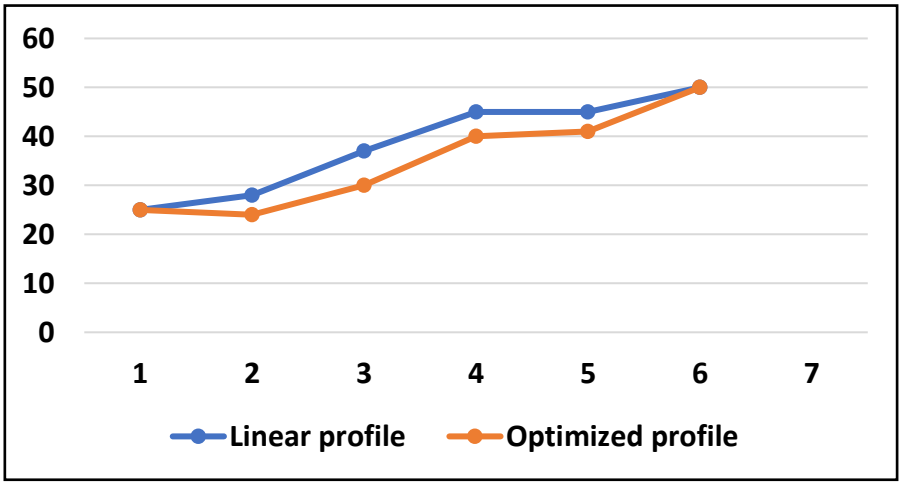

Fig. 4: The Antisolvent Addition Affects the Particle Size Distribution

4. DISCUSSIONS

Both a growth rate curve and a schematic solubility curve are provided to compare the behaviour of various solvents and to estimate various kinetic parameters. You can utilise Solubility Screen results in your search for cooling crystallisation or antisolvent alternatives to pick suitable solvents. An investigation into the effect that particle size distribution has on seed transformation has been carried out. The result of tests to determine the effect of cooling rate on the distribution of crystal sizes (CSD) The temperature is gradually lowered at the beginning of the cooling process and then rapidly lowered at the end. Controlled supersaturation results in a population shift toward larger particle sizes, avoiding excessive nucleation. Experimental results show the effect on the Crystal Size Distribution of varying rates of antisolvent addition (CSD). The optimal antisolvent profile regulates the crystal size distribution by maintaining a consistent amount of supersaturation. The solubility curve is steep at the beginning of the process, and the antisolvent is introduced very slowly to avoid excessive supersaturation of the solution.

5. CONCLUSION

Crystallization operations can benefit from the most advanced analytical techniques now available. An approach for developing crystallisation processes that are reliable has been described. For the purpose of planning, developing, and executing crystallisation experiments, this methodology is the best option available. The crystallisation process development approach is broken down into seven steps, each of which focuses on a different aspect of the planning, screening, optimization, and verification processes. When applied correctly, this methodology helps to speed up the process of developing novel pharmaceutical processes by gaining a better understanding of important process factors and their impact on product attributes.

REFERENCES

1. P. V. Patel “Liquid Crystal Drug Delivery System” International Journal of Pharmaceutical and Applied Sciences, Vol 1, issue (1), Page 118-123,2010
2. Zafar Alam Mahmood. “In vitro microscopic study of mono sodium urate monohydrate crystals growth patterns”. J Pharm Sci Innov. Vol 4, Issue (6), Page 295-297,2015
3. Hasan M, “In vitro microscopic study of calcium hydrogen phosphate dihydrate crystals growth patterns”. World J Pharm Sci, Vol 4, Issue (1), Page 64-67,2016.
4. Lagerwall JP, Scalia G. “A new era for liquid crystal research: applications of liquid crystals in soft matter nano-, bio-and microtechnology”. Current Applied Physics, vol 12, issue (6), page 1387-412,2012.
5. Sadhana S, Vivek R, Iftequar S. “Liquid crystals pharmaceutical application”. J International Pharmaceutical Research & Allied Sciences. Vol 1, issue (1), page 6-11,2012.
6. Zhao XY, Zhang J, Zheng LQ, Li DH. “Studies of cubosomes as a sustained drug delivery system”. Journal of dispersion science and technology. Vol 25, issue (6), Page 795-9,2005.

7. Dierking I, Al-Zangana S. “Lyotropic liquid crystal phases from anisotropic nanomaterials”. Nanomaterials. Vol 7, issue(10), page 305,2017.
8. Zhang S, Kumar S. “Carbon nanotubes as liquid crystals”. Small. Vol 4, issue (9), Page 1270-83,2008.
9. Iwabata K, Sugai U, Seki Y, Furue H, Sakaguchi K. “Applications of biomaterials to liquid crystals”. Molecules. Vol 18, issue (4), page 4703-17,2013.
10. Dierking I. “A review of polymer-stabilized ferroelectric liquid crystals”. Materials. Vol 7, Issue (5), page 3568-87,2014.
11. Chandrasekhar S. “Discotic liquid crystals. A brief review”. Liquid Crystals. Vol14, issue (1), page 3-14,1993.
12. Wadhawan, V. (2007). “Growth Rate Anisotropy and Absorption Studies on β-BaB2O4 Single Crystals Grown by the Top-seeded Solution Growth Technique”. Optical Materials , vol 29,issue (1), Page 801-805,2007
13. Van Vleet, “In situ, time-resolved, and mechanistic studies of metal−organic framework nucleation and growth”. Chem. Rev. Vol 118, issue (1), Page 3681–3721,2018.
14. Hafizovic, “The inconsistency in adsorption properties and powder XRD data of MOF-5 is rationalized by framework interpenetration and the presence of organic and inorganic species in the nanocavities”. J. Am. Chem. Soc. Vol 129, issue (1), Page 3612–3620,2007.
15. Zheng, C.M “Microstructural study of formation mechanism of metal-organic framework MOF-5”. CrystEngComm Vol 16, issue (1), Page 1064–1070,2014.
16. Greer, H.F.; Liu, Y.H.; Greenaway, A.; Wright, P.A.; Zhou, W.Z. “Synthesis and formation mechanism of textured MOF-5”. Cryst. Growth Des. 2016, Vol 16, issue (1), Page 2104–2111,2016
17. Chen, J.L “Chemistry of hydrolysis of FeCl3 in the presence of phosphate to form hematite nanotubes and nanorings”. Cryst. Growth Des. Vol 17, issue (1), Page 5975–5983,2017.
18. Yang, X.F “Formation mechanism of CaTiO3 hollow crystals with different microstructures”. J. Am. Chem. Soc, Vol 132, issue (1), Page 14279–14287,2010.
19. Zhan, H.Q “Correlation between multiple growth stages and photocatalysis of SrTiO3 nanocrystals”. J. Phys. Chem. C, Vol 119, issue (1), Page 3530–3537,2015.
20. Zhan “Multiple nucleation and crystal growth of barium titanate. Cryst”. Growth Des. 2012, Vol 12, issue (1), Page 1247–1253,2012.