LOKNETE SHREE DADASAHEB PHARATE PATIL COLLEGEOF

PHARMACY, MANDAVGOAN PHARATA

TAL - SHIRUR , DIST – PUNE. MAHARASHTRA

A REVIEW ON SOLID DOSAGE FORM

Department of Pharmaceutics

POOJA BHASKAR DEHADE

AUTHERS NAME:

Dr. Hemant V Kamble

Dr. Vivek M Satpute

Prof. Santosh A Waghmare

ABSTRACT:

Spouted beds (SBs) have a long history of successful applications for preparation of solid dosage forms of pharmaceuticals. The well-known versatility of SBs, provided by different design and operational factors, andtheir efficientmixing of solids allow for engineering oftechnological characteristics ofpharmaceutical solid forms. Particle properties like morphology, size, porosity, flowability, and dissolution rate can be improved by managing geometric and operational conditions for spouting. Drying is probably the most disseminated operation for pharmaceutical processing in SBs, and many studies have investigated drying of medicinal plant extracts such as achiote (Bixa orellana sp.), guarana (Paullinia cupana sp.), passion flower (Passiflora alata D.), and rosemary (Rosmarinus officinalis L.) with excellent pharmacotechnical and stability results. Another important application is coating of tablets and gelatin capsules, and previous studies have shown that SBs and spout–fluid beds may be advantageous over traditional pan coating, especially for polymeric film coating. Recently, an alternative process for improving drug bioavailability has involved preparation of -cyclodextrin inclusion complexes in SBs. The first study to propose SBs for this pharmaceutical application explored the advantage of obtaining solid forms of inclusion complexes in just one step, and obtained expressive increases in drug solubility. The technique has been applied in subsequent studies on inclusion complexes of the medication carvedilol and uxi (Endopleura uchi L.) extracts. Lubrication plays a key role in successful manufacturing of pharmaceutical solid dosage forms; lubricants are essential ingredients in robust formulations to achieve this. Although many failures in pharmaceutical manufacturing operations are caused by issues related to lubrication, in general, lubricants do not gain adequate attention in the development of pharmaceutical formulations. In this paper, the fundamental background on lubrication is introduced, in which the relationships between lubrication and friction/adhesion forces are discussed.

KEYWORDS : Lubricants; Boundary Lubrication; Magnesium Stearate; Friction; Adhesion; The Maximum Compression Pressure; Ribbon and Tablet Density; Chemical Incompatibility, Degradaation schemes, equations and rate constants, effect of moisture 0 Moisture effect-decomposition of solid dosage forms

INTRODUCTION

Since their first mention in engineering literature for fluidization of wheat (Mathur & Gishler, 1955), spouted beds (SBs) have been applied to mixing, granulation, coating, and drying of coarse particles that are inadequate for typical fluidization (Epstein & Grace, 2011). Particles larger than 1 mm tend to develop undesirable fluidization with anomalous regimes and instabilities, like slugging and channeling. The SB is an excellent gas–solid contactor with many geometric and operational variables (Epstein & Grace, 1997), which allow for versatility in engineering design and operation (Marreto, Freire, & Freitas, 2006). Although many studies have been developed for SB applications for specialty chemicals (Buczek, 2013), in agriculture (Viswanathan, Lyall, & Raychaudhuri, 1986), and to biotechnological products (Silva & Yang, 1998; Webb, Fukuda, & Atkinson, 1986) and pharmaceuticals (Marreto et al., 2006), attempts to scale-up these processes have shown that SBs have size limitations (He, Lim, & Grace, 1997).

A lubricant, an additive to reduce friction, is an essential component of a drug formula since lubrication is often required to ensure the success of pharmaceutical manufacturing. Historically, use of animal fats as lubricants to reduce friction in transportation can be traced back to Egyptian time. However, the development of modern tribology, which is the study of friction and lubrication, did not gain ground until Frank P. Bowden established a research laboratory on friction, lubrication, and bearings in Melbourne, Australia during World War II [1]. Since then, a systematic study on friction and lubrication, termed “tribology”, was initiated. Lately, due to the development of instrumentations in surface and interfacial characterization, and force measurements as well as the improved

understanding between friction and adhesion force, tribology has been developed into an active research field. In particular, in the pharmaceutical industry, the application of lubrication or tribology in drug development has become increasingly important for developing a successful manufacturing process [2]. For pharmaceutical operations such as blending, roller compaction, tablet manufacturing, and capsule-filling, lubrication is essential in order to reduce the friction between the surfaces of manufacturing equipment and that of organic solids as well as to ensure the continuation of an operation [3]. Pharmaceutical lubricants are the agents added to tablet and capsule formulations in a very small quantity (usually 0.25%–5.0%, w/w) to improve the powder processing properties of formulations. Albeit a fairly small amount, lubricants play important roles in manufacturing; they decrease friction at the interface between a tablet's surface and the die wall during ejection so that the wear on punches and dies are reduced; they prevent sticking of tablets to punch faces as well as sticking of capsules to dosators and tamping pins. In terms of powder flow, lubricants can improve the flowability of blends and aid unit operations. For instance, for the blending of active pharmaceutical ingredients (APIs) of small particles with other excipients, the adhesion force between particles can significantly reduce the powder flowability by increasing inter-particle friction; poor flow can cause insufficient mixing of the blends (content uniformity) and rat-holing in the hopper of a tablet press (segregation issue), impacting both product quality and operation. To overcome these issues, lubricants are added (glidants) to enhance powder flow by reducing the inter-particle friction. Regarding lubrication agents, although magnesium stearate and stearic acid are the most frequently used lubricants in the pharmaceutical industry, there are other lubricants in use as well [4]. Moreover, because technologies for monitoring the dynamics of powder flow during manufacturing processes have been improved, the impact of lubricants on powder dynamics and compact properties are now better understood. All of this will be summarized in this paper.

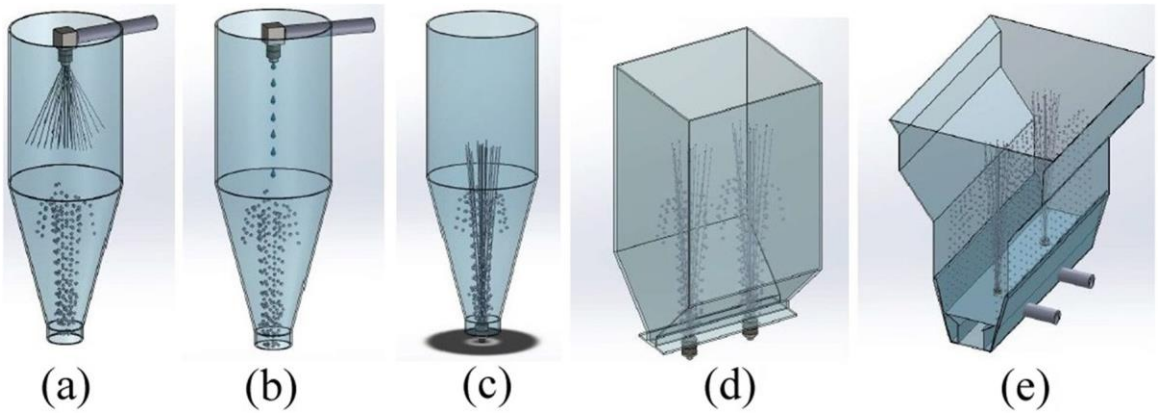

Fig. 1. Different spouted bed configurations and geometries applied to pharmaceutical processing: (a) conventional SB with top spray feed; (b) conventional SB with top drip feed; (c) conventional SB with bottom spray feed; (d) slot-rectangular SB with bottom spray feed; and (e) slot-rectangular SB with adjustable slot width (Glatt GmbH, Germany).

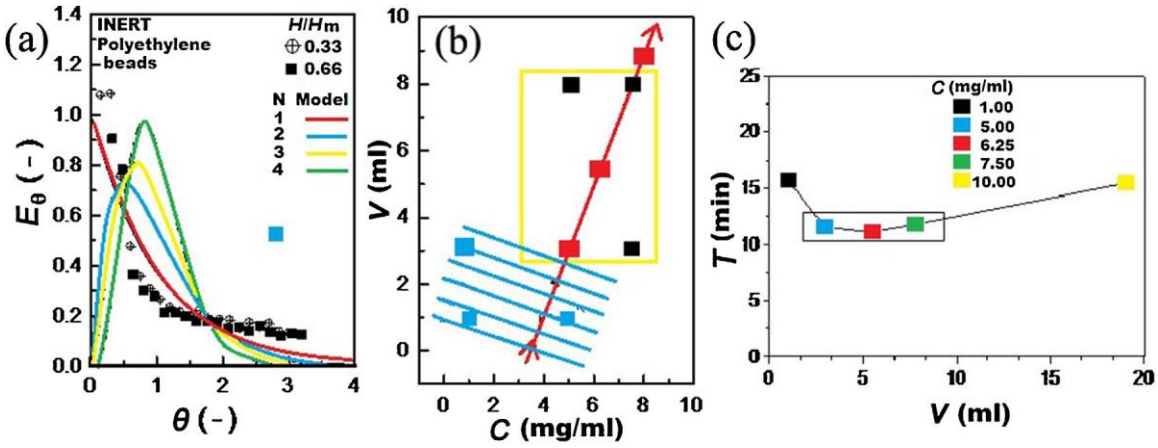

Fig. 2. Residence time distributions during drying of salt solutions in spouted beds: (a) residence time distributions and continuous stirred-tank reactor models, (b) exploratory experimental design to determine best the stimulus-response methodology, and (c) mean residence time along the steepest ascent line of the exploratory design.

- **Drying**

Drying of a pharmaceutical is essential to ensure product stabil- ity, efficacy, and quality (Marquele et al., 2006; Marreto et al., 2006; Pakowski & Mujumdar, 1995). Spray drying and freeze-drying are the methods most frequently used for drying pharmaceutical prod- ucts (Marquele, Stracieri, Fonseca, & Freitas, 2006; Pakowski & Mujumdar, 1995; Reis, Costa, Tacon, Teixeira, & Freitas, 2017). Spray drying allows for precise control of product properties, such as particle size, flowability, bulk density, and water content, and is suitable for any production scale from a few grams per hour on a laboratory scale to thousands of tons per hour at full industrial scale (Filkova & Mujumdar, 1995; Souza, Tacon, Correia, Bastos, & Freitas, 2007). The main advantage of freeze-drying is its low operation temperature, which decreases the chance of thermal degradation of the actives (Tang & Pikal, 2004; Walters et al., 2014). However, both methods have limitations: spray drying cannot be applied to sticky raw materials, and freeze-drying has long processing times and high operational costs (Walters et al., 2014). Although the choice of a drying method for pharmaceuticals must be based on the product physico-chemical properties and thermal sensitivity (Markowski, 1993; Marreto et al., 2006; Walters et al., 2014), the application of SBs to drying has recently been the focus of extensive research.

Coating:

The coating of solid dosage forms has gained distinction among pharmaceutical processes because it can add new functionalities to old dosage forms, such as tablets, capsules, and pellets (Qiu, 2009). Sugar solutions are used to coat tablets to improve their appearance, mechanical resistance, and taste (Porter, Sackett, & Liu, 2009). For decades, pan coating has been the method of choice for sugar coating tablets (Lachman et al., 1976). The development of polymers for use in health care products in the early 1950s cre- ated demand for new equipment because traditional pan coaters had low

aeration profiles and low drying capacities and were not efficient for application of these polymers (Brady, During, & Shang, 2009). Consequently, Professor Dale E. Wurster developed and patented an air-suspended tablet coating system (Wurster, 1953) that became known as the Wurster chamber (Seville et al., 2011).

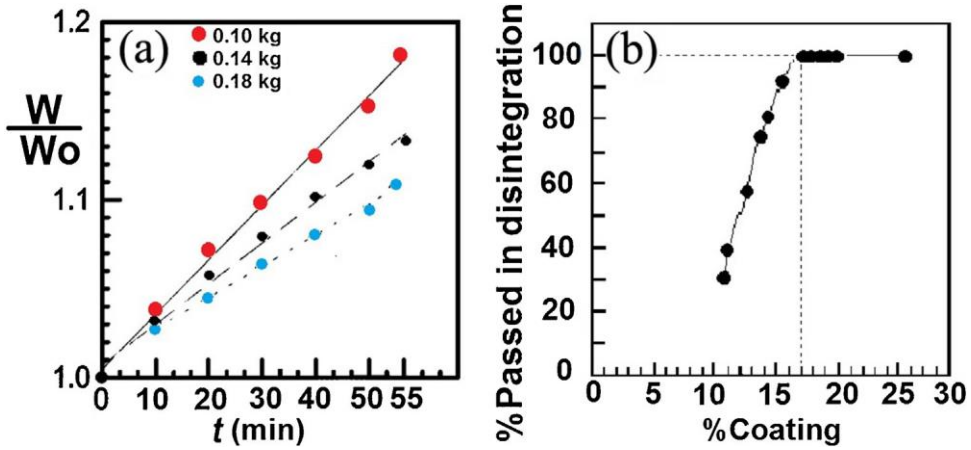

Fig 3: Hard gelatin capsules coated in a spouted bed: (a) mass gain as a function of coating time for different bed loads, and (b) percentage of capsules passing gastric resistance test as a function of the coating thickness (%coating, mass gain). (Source: Shuhama et al., 2003).

Lubrication

In general, there are four lubrication mechanisms: hydrodynamic lubrication, elastohydrodynamic lubrication, mixed lubrication, and boundary lubrication [1,5]. As their names implies, the former three mechanisms are related to the usage of liquid lubricants to some extent. In the pharmaceutical industry, boundary lubrication is the most common mechanism functioning in unit operations [2]. For boundary lubrication, a lubricant typically forms layers/film between surfaces or at interfaces to reduce friction, where the penetration of the lubricant into surface asperities occurs. Structurally, the lubricants commonly used for boundary lubrication are long chain molecules with active end-groups

such as stearic acid and its metallic salts. The typical end-groups include: (1) –OH (long chain alcohol); (2) –NH2 (long chain amine); (3) –COOH (long chain fatty acids); and (4) metal ions such as Mg2+. The molecules with these end-groups can be readily adsorbed on the surfaces of metals or other particles to form an oriented monolayer or multilayers. The layers formed prevent further contact between the intended surfaces and powder particles. The efficiency of a boundary lubricant is measured by the extent to which these films can mask the field of force of the underlying surface [1]. In other words, a lubricant film such as the film of magnesium stearate needs to be sufficiently thick to cover the surface, typically a few layers. In addition, the breaking down of the lubricant film plays a significant role so that the motion of lubricated surface is facilitated. This will be illustrated by our discussion on the dihydrate of magnesium stearate, which in general gives the best lubrication efficiency due to its layered structure.

Conclusion

The drying of medicinal plant extracts in CSB dryers was eval- uated with two of the most important Brazilian plants. The APIs found in these plants were used as chemical markers for evaluation of the drying performance and product quality. Caffeine and bixin, a psychoactive alkaloid and a carotenoid, respectively, showed that SBs provide a range of operational conditions that allow for good preservation of principle APIs and adequate water content in dry powders. For both plant materials, degradation of the API increased sharply at a specific temperature. The results demonstrate that each API needs to be studied to validate the CSB drying method. The CSB process for annatto drying is competitive compared with commercial methods.

Acknowledgement

The authors are grateful to the management of Loknete Shri Dadasaheb Pharate Patil College of Pharmacy, Mandavgoan Pharata, for providing the facilities and access to online resources needed to conduct the literature review. The author is also grateful to Dr.Amol Lokhande for his valuable guidance.

Summary

In summary, there are many factors to be considered for selecting an appropriate lubricant for preparing solid dosage forms including: low shear strength, being able to form a durable layer covering the surface/particles, non-toxic, chemically compatible with APIs and other components in the formulation, low batch to batch variability, and having minimum adverse effects on the performance of the finished dosage forms. In addition, the optimal concentration and mixing time are also needed to be taken into consideration when selecting a lubricant because both of these two parameters greatly impact the performance of pharmaceutical products and processes.

The drying of microcapsules in a CSB is an interesting alternative

to spray drying, and allows for unique drug release properties. Drug recovery results from SB dried microcapsules demonstrate that SB dryers may be useful to prepare modified release systems for highly-soluble drugs. However, the reason for the peculiar behavior of CSB dried microcapsules is still not clear and further research is required on this topic. The preparation of drug inclusion complexes in βCD by SB absorption is a new and promising technique that may present an economical and viable alternative to spray drying. In this paper, the fundamentals of lubrication and the action mechanisms of lubricants in typical pharmaceutical manufacturing processes have been

reviewed; the role of lubricants in improving pharmaceutical operations by reducing the adhesion forces between powder/equipment as well as particle/particle in terms of wall friction and inter-particle friction has been summarized.

Reference

1. Bowden, F.P.; Tabor, D. The Friction and Lubrication of Solids; Clarendon Press: Oxford, UK, 2001.

2. Wang, J.; Wen, H.; Desai, D. Lubrication in tablet formulations. Eur. J. Pharm. Biopharm. 2010,

75, 1–15.

3. Bolhuis, G.K.; Hölzer, A.W. Lubricant Sensitivity. In Pharmaceutical Powder Compaction Technology, 1st ed.; Alderborn, G., Nyström, C., Eds.; Marcel Dekker, Inc.: New York, NY, USA, 1996; pp. 517–560.

4. Goldberg, R.; Klein, J. Liposomes as lubricants: Beyond drug delivery. Chem. Phys. Lipids 2012,

165, 374–381.

5. Faghihnejad, A.; Zeng, H. Fundamentals of Surface Adhesion, Friction, and Lubrication. In Polymer Adhesion, Friction, and Lubrication; Zheng, H., Ed.; Wiley & Sons, Inc.: Hoboken, NJ, USA, 2013; pp. 1–57.

6. Israelachvili, J.N. Intermolecular and Surface Forces, 3rd ed.; Elsevier: Burlington, MA, USA, 2011; pp. 469–499.

7. Pietsch, W. Size Enlargement by Agglomeration. In Handbook of Powder Science & Technology, 2nd ed.; Fayed, M.E., Otten, L., Eds.; Chapman & Hall: New York, NY, USA, 1997; pp. 202–295.

8. Butt, H.J.; Graf, K.; Kappl, M. Physics and Chemistry of Interfaces; Wiley-VCH: Weinheim, Germany, 2003.

9. Bowden, F.P.; Tabor, D. Friction: An Introduction to Tribology; Doubleday & Company, Inc.: Garden City, NY, USA, 1973.

10. Schulze, D. Powder and Bulk Solids: Behavior, Characterization, Storage and Flow; Springer-Verlag: Heidelberg, Germany, 2008.

11. Gethin, D.T.; Solimanjad, N.; Doremus, P.; Korachkin, D. Friction and Its Measurement in Powder-Compaction Processes. In Modelling of Powder Die Compaction; Brewin, P.R., Coube, O., Doremus, P., Tweed, J.H., Eds.; Springer-Verlag: London, UK, 2008; pp. 105–129.

12. Zimmermann, I.; Eber, M.; Meyer, K. Nanomaterials as flow regulators in dry powders.

Z. Phys. Chem. 2004, 218, 52–102.

13. Miller, T.A.; York, P. Pharmaceutical tablet lubrication. Int. J. Pharm. 1988, 41, 1–19.

14. O'Rourke, S.E.; Morris, R.H. Metallic stearate: A review of their function and use as release agents for rubber compounds. Prog. Rubber Plast. Technol. 1998, 14, 238–247.

15. Abramovici, B.; Gromenil, J.C.; Molard, F.; Blanc, F. Comparative study on the lubricating properties of a new additive: The glycerol tribehenate (Compritol® 888) compared to magnesium stearate. Bull. Tech. Gattefosse 1985, 78, 75–85.

16. Aoshima, H.; Miyagisnima, A.; Nozawa, Y.; Sadzuka, Y.; Sonobe, T. Glycerin fatty acid esters as a new lubricant of tablets. Int. J. Pharm. 2005, 293, 25–34.

17. Jannin, V.; Bérard, V.; N'Diaye, A.; Andrés, C.; Pourcelot, Y. Comparative study of the lubricant performance of Compritol® 888 ATO either used by blending or by hot melt coating. Int. J. Pharm. 2003, 262, 39–45.

18. Dawoodbhai, S.S.; Chueh, H.R.; Rhodes, C.T. Glidants and lubricant properties of several types of talcs. Drug Dev. Ind. Pharm. 1987, 13, 2441–2467.

19. Lapeyre, F.; Cuiné, A.; Chulia, D.; Vérain, A. Quantitative evaluation of tablet sticking anti-adherent properties of some tablet lubricants. STP Pharma 1988, 4, 106–110.

20. Okoye, P.; Wu, S.H.; Dave, R.H. To evaluate the effect of various magnesium stearate polymorphs using powder rheology and thermal analysis. Drug Dev. Ind. Pharm. 2012, 38, 1470–1478.

21. Bracconi, P.; Andrés, C.; Ndiaye, A. Structural properties of magnesium stearate pseudo-polymorphs: Effect of temperature. Int. J. Pharm. 2003, 262, 109–124.

22. Rao, K.P.; Chawla, G.; Kaushal, A.M.; Bansal, A.K. Impact of solid-state properties on lubricant efficacy of magnesium stearate. Pharm. Dev. Technol. 2005, 10, 423–437.

23. Ertel, K.D.; Carstensen, J.T. Chemical, physical, and lubricant properties of magnesium stearate.

J. Pharm. Sci. 1988, 77, 625–629.

24. Barra, J.; Somma, R. Influence of the physicochemical variability of magnesium stearate on its lubricant properties: Possible solutions. Drug Dev. Ind. Pharm. 1996, 22, 1105–1120.

25. Dansereau, R.; Peck, G.E. The effect of the variability in the physical and chemical properties of magnesium stearate on the properties of compressed tablets. Drug Dev. Ind. Pharm. 1987, 13, 975–999.

26. Soebagyo, S.S. The effect of the particle size of magnesium stearate on the dissolution of dexamethasone from interactive mix tablet. Maj. Farm. Indones. 1994, 5, 52–58.

27. Kushner, J.I.V.; Langdon, B.A.; Hiller, J.I.; Carlson, G.T. Examining the impact of excipient material property variation on drug product quality attributes: A quality-by-design study for a roller compacted, immediate release tablet. J. Pharm. Sci. 2011, 100, 2222–2239.

28. Morin, G.; Briens, L. The effect of lubricants on powder flowability for pharmaceutical application.

AAPS PharmSciTech 2013, 14, 1158–1168.