HOSTED BY

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ajps

Review

A classification system for tableting behaviors of binary powder mixtures

Changquan Calvin Sun *

Pharmaceutical Materials Science and Engineering Laboratory, Department of Pharmaceutics, College of Pharmacy, University of Minnesota

ARTICLE INFO

Article history:
Received 1 September 2015
Received in revised form 22 October 2015
Accepted 13 November 2015
Available online 2 February 2016

Keywords:
Powder
Mixture
Tensile strength
Tabletability
Classification system
Compaction

ABSTRACT

The ability to predict tableting properties of a powder mixture from individual components is of both fundamental and practical importance to the efficient formulation development of tablet products. A common tableting classification system (TCS) of binary powder mixtures facilitates the systematic development of new knowledge in this direction. Based on the dependence of tablet tensile strength on weight fraction in a binary mixture, three main types of tableting behavior are identified. Each type is further divided to arrive at a total of 15 sub-classes. The proposed classification system lays a framework for a better understanding of powder interactions during compaction. Potential applications and limitations of this classification system are discussed.

1. Introduction

Tabletability is the capacity of a powdered material to be transformed into a tablet of specified strength under the effect of compaction pressure [1,2]. It may be represented by a plot of tablet tensile strength vs. compaction pressure. Since pharmaceutical tablets usually contain multiple ingredients, the ability to predict tabletability of a powder mixture from individual components is of both fundamental and practical importance to pharmaceutical industry.

A mark of empirical formulation development is the choice of formulation composition based on personal preference and previous experience with other drugs. Unfortunately, the same excipient matrix that worked for some active pharmaceutical ingredients (API) may not be appropriate, much less optimum, for another API because the properties of different APIs can differ profoundly and drug loading likely is also different. Although it is possible to prepare a series of powder mixtures for a new drug candidate and quantify their tabletability in turn, this screening approach is time and resource intensive for formulation development. In contrast, formulation design based on an understanding of tableting performance of drug and individual excipients as well as their interactions would be much more efficient. In this context, the ability to reliably predict tabletability of a mixture based on that of constituting components is critical. Hence, in addition to the consideration of stability, flowability, and other important pharmaceutical properties, the selection of excipients should be also based on their mechanical properties. This approach allows better

* 9-127B Weaver-Densford Hall, 308 Harvard Street S.E., Minneapolis, MN 55455, USA. Tel: +1 612 624 3722; fax: +1 612 626 2125.
E-mail address: sunx0053@umn.edu.

Peer review under responsibility of Shenyang Pharmaceutical University.
http://dx.doi.org/10.1016/j.ajps.2015.11.122

accommodation of unique properties of the API, rather than by trial and error, to deliver an overall superior powder mixture (formulation) that can be processed and manufactured robustly. This is particularly important for truly realizing the quality-by-design.

Efforts have been made to study tableting properties of mixtures [3–21]. At a high level, these studies can be divided according to the tableting property they focused on, e.g., compressibility (porosity vs. pressure) [22] and compactibility (tensile strength vs. porosity (or relative density)) [23,24]. Compressibility and compactibility are fundamental properties that influence powder tabletability [25,26]. However, tabletability is of practical importance because it describes the relationship between the process parameter, i.e., pressure, and an important property critical to tablet quality, i.e., mechanical strength. Therefore, the ability to predict tableting performance of mixtures from those of individual components is useful, but not yet attained. Accurate predictions would require the access to a large set of data that accurately describes tabletability of excipients and their mixtures. A useful step in achieving such a goal is to develop a classification system for tableting behaviors of binary powder mixtures, which helps to systematically describe data and facilitate communication among scientists.

Perhaps it is with this vision that a simple classification was introduced [27]. This classification, although useful, is not adequate to describe diverse types of tabletability observed so far or those that can possibly occur. In this report, a more comprehensive tableting classification system (TCS) for binary powder mixtures is proposed based on theoretical considerations. Characteristics of each system are described. Examples are given when possible. It is hoped that a refined TCS will serve as an initial step toward a more fundamental understanding of powder interactions during compaction. The adoption of TCS is expected to expedite the development of in-depth understanding of powder compaction of mixtures.

2. Classification system

The classification of tableting behaviors of powder mixtures is based on tensile strength of tablet compressed under a constant compaction pressure. For practical reasons, tensile strength is plotted against weight fraction only (alternatives are volume fraction and molar fraction). When tensile strengths of two powders, A and B, are different, A is always used to represent the powder with a lower tensile strength. The weight fraction axis is always expressed as amount of the powder exhibiting higher tensile strength. It is possible that under different compaction pressures, the same mixture system may behave differently and fall into a different class because tablet tensile strength depends on pressure differently for different powders.

2.1. Type I

Type I behavior is exhibited if tensile strengths of tablets from individual components are non-zero and if they differ significantly (>10%) (Fig. 1). Tableting behavior of binary mixture of most fillers and binders exhibit Type I behavior. Type I behavior may be further divided into seven sub-classes based on the interaction between the two components.

Type I(a) exhibits ideal behavior, where tablet tensile strength depends on the weight fraction linearly. A straight line may be drawn between points A and B in Fig. 1. Both *Type I(b)* and *I(c)* exhibit positive deviations from the ideal line. *Type I(b)* is assigned when tensile strength of tablets of mixtures does not exceed that of *B*. Otherwise, *Type I(c)* is assigned. In other words, Type I(c) shows positive deviation so much that some of the mixtures exhibit tablet tensile strength higher than both constituent powders. Similarly, Type *I(d)* is assigned when tensile strength of mixtures negatively deviates from the ideal line but always lies between those of A and B, and Type *I(e)* is assigned to systems where negative deviations lead to tensile strength lower than that of A.

Types I(f) and I(g) are characterized by a constant tablet tensile strength (at either low or high end of the curve) over a certain weight fraction of the mixtures (Fig. 1). Outside of this range, tablet tensile strength depends on composition of mixtures. *Type I(f)* is identified when the flat part of the plot falls in the region where powder B is a minor component (weight fraction <0.5). *Type I(g)* is when the flat part of the plot falls in the region where powder *A* is a minor component on a weight basis. Depending on the shape of the changing part of the plot, more

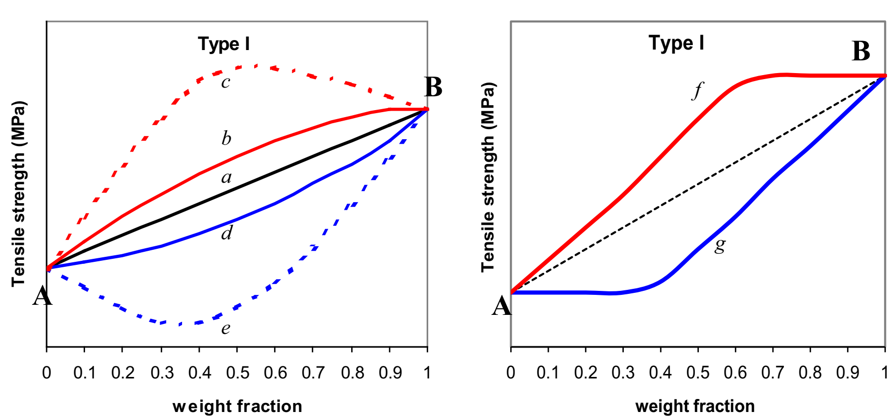

Fig. 1 – Type I behavior of binary powder mixtures: (a) ideal; (b) mild positive deviations from ideality; (c) severe deviations from ideality; (d) mild negative deviations from ideality; (e) severe negative deviations from ideality; (f) tensile strength increases with increasing powder *B* in mixtures up to a critical composition and subsequently leveled off; (g) tensile strength remains constant up to a critical composition and subsequently increases.