Three-Dimensional Printing in Pharmaceutics: Promises and Problems

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ABSTRACT: Three-dimensional printing (3DP) is a rapid prototyping (RP) technology. Prototyping involves constructing specific layers that uses powder processing and liquid binding materials. Reports in the literature have highlighted the many advantages of the 3DP system over other processes in enhancing pharmaceutical applications, these include new methods in design, development, manufacture, and commercialization of various types of solid dosage forms. For example, 3DP technology is flexible in that it can be used in applications linked to linear drug delivery systems (DDS), colon-targeted DDS, oral fast disintegrating DDS, floating DDS, time controlled, and pulse release DDS as well as dosage form with multiphase release properties and implantable DDS. In addition 3DP can also provide solutions for resolving difficulties relating to the delivery of poorly water-soluble drugs, peptides and proteins, preparation of DDS for high toxic and potent drugs and controlled-release of multidrugs in a single dosage forms. Due to its flexible and highly reproducible manufacturing process, 3DP has some advantages over conventional compressing and other RP technologies in fabricating solid DDS. This enables 3DP to be further developed for use in pharmaceutics applications. However, there are some problems that limit the further applications of the system, such as the selections of suitable excipients and the pharmacotechnical properties of 3DP products. Further developments are therefore needed to overcome these issues where 3DP systems can be successfully combined with conventional pharmaceutics. Here we present an overview and the potential 3DP in the development of new drug delivery systems. © 2008 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 97:3666–3690, 2008

Keywords: three-dimensional printing; pharmaceutics; drug delivery systems/devices; controlled release; solid dosage forms

INTRODUCTION

Three-dimensional printing (3DP) is a relatively new rapid prototyping (RP) technique. The system was first developed at the Massachusetts Institute of Technology (1992) and is based on computer-aided design (CAD) models that are manipulated by a terminal computer. Briefly the

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construction of 3DP systems involves a very simple layer-wise process that can be rapidly applied. A typical process is shown in Figure 1. Firstly a layer of powder is spread onto the powder-bed on which the prototype is to be created. A print head, similar to that used in ink printing is driven by an *X*–*Y* orientation system to eject binding materials onto the powder. This produces the base layer that relates to a specified CAD pattern. The powder-bed is driven by the piston rod in the *Z* vertical orientation, this is then lowered into a predetermined thickness layer and the process is repeated until the required 3D shape has been constructed. After treatment, unbound powder is removed, leaving the fabricated part.[1–3]

3DP has unprecedented flexibility. It can accommodate many geometrical outlines and can be made from many materials, such as ceramics, metals, polymers, and composites to create the appropriate geometry. The system allows control over the material composition, microstructure and surface texture, this flexibility has many attractions within the pharmaceutics field. 3DP can offer many novel strategies and approaches for the research and development of the controlled-release (CR) drug delivery systems (DDS) and so is becoming of much interest.

A survey of open publications relating to 3DP (the research tip is "three-dimensional printing" within "Abstract, Title, Keywords") and publications linked to both 3DP and DDS (the research tip is "three-dimensional printing" within "Full text" And "drug delivery systems" within "Full text") in the past several years was conducted based on Elservier Science Direct in August 11, 2007. The results are given in Figure 2. The data clearly demonstrate the gradually increasing trends of research both on 3DP and in the application of 3DP in pharmaceutics.

Recently engineering tablets with complex inner structures, special geometries, variations of materials and active agents, surface texture and many types of DDS have been developed using 3DP. For example oral CR systems, drug delivery microchip, CR pills, implantable DDS, rapidly dissolving DDS, and multiphase release DDS[4–10] have been developed. Moreover, 3DP has many manufacturing advantages over conventional compressing technologies in fabricating solid dosage forms and can offer other opportunities in dealing with some difficulties in pharmaceutics. It is expected that 3DP technique could provide new strategies for developing of novel pharmaceutical products. However there are some problems that limit the further applications of 3DP and must be resolved before the full use of 3DP DDS in clinical applications can be achieved.

OPPORTUNITIES

Most of the conventional tablets rely on the chemical and physical properties of the excipients

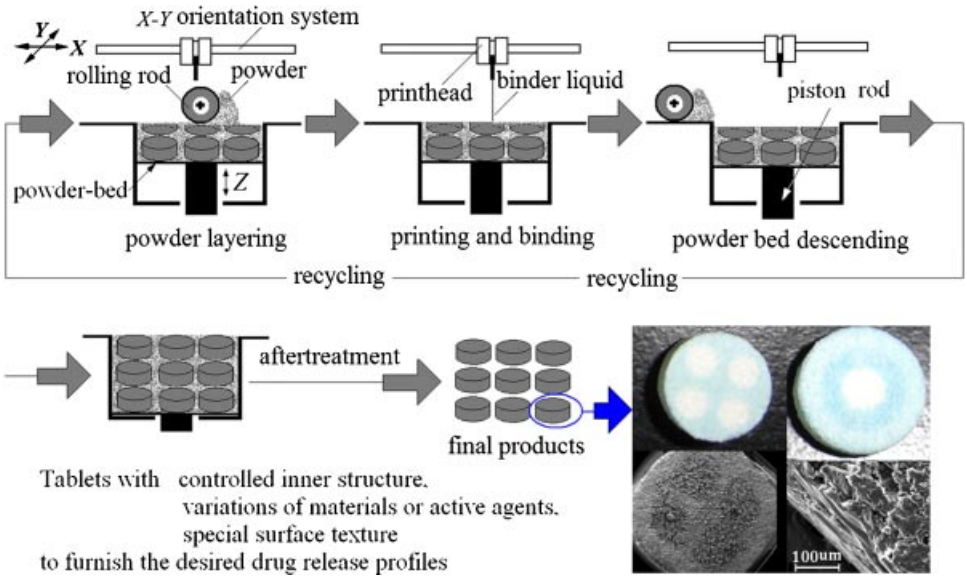

Figure 1. 3DP process (adopted from Ref. 3 and revised).