USAGE OF 3D PRINTER TECHNOLOGY IN MEDICAL AND PHARMACEUTICAL FIELDS: A REVIEW

ABSTRACT

Along with the developing technology, 3D printers have found broad applications in medical and pharmaceutical fields. Precise digital control over layer by layerprinting given by 3D printers allows drugs, cosmetics and medical devices like prostheses to be personalized for treatment.Additionaly, the physical structure of 3D printed productsand theirvisualization is effective on surgical planning, educational and research applications alleviating the endeavior of surgeons,students and scientists, respectively. Since FDA's first 3D printed drug approval in 2015, the research for new approaches has been growing although the manufacturers need regularity certainty.As for 3D organ printing, it remains the great expectation albeit some attempts.This review is aimed at giving brief explanations about 3D printing achievements and applications in medical and pharmaceutical fields.

Keywords: Biomedical, Medicine,Bioprinting,Personalized treatment,Cosmetics, 3D Printing

INTRODUCTION

The development of 3D printer technology, which started in the 1980s, and the growth of the market have gained importance in recent years. Nowadays, the usage of 3D printer technology with three-dimensional (3D) printing has been started to be used in biomedical and cosmetics including pharmaceutical fields, and the first steps have been taken in the cosmetic industry (Ashraf et al., 2018, Gross et al., 2014, Kandarova et al., 2009, Yapar, 2016).

The field of health is on its way to becoming one of the most important areas of use in 3D printing and printers. Major usage examples include the production of biomodels (artificial models of human body parts, such as bone, dental prosthesis, etc.). The development of artificial models for different individual anatomy of humans provides many benefits in the field of treatment enabling more accurate diagnosis,better execution of the planning and testing stages, more effective orientation during the operation that improves the quality and accuracy, testing opportunity of new medical methods and technologies and research, training and practice activities to be carried out more effectively.3D printers play an active role in the design and manufacture of personalized implants, prostheses and artificial organs, and production of personalized medical materials such as hearing aids, scaffolding and mask. In addition, 3D printer technology enables the production of sensitive systems / devices in the delivery of medicines. By means of 3D printers, human tissues and organs can be produced in layer by layer using artificial human tissue as bio-raw

material(bioprinting).These raw materials can be obtained by treating live human cells using various chemicals and methods. Bioprinting has a remarkable potential for personalized drug development, treatment-related tests, medical research, wound healing, and even organ transplants (Gross et al., 2014, Kandarova et al., 2009, Karagöl, 2015).The application of 3D printing in health products offers some advantages such as; customization and personalization of medical products, medicinesand equipment; cost-effectiveness; increased productivity; the demonstration of design and manufacturing; training for health education(Ventola, 2014).

In the field of cosmetics, following the use of 3D human skin models in the efficacy and safety tests of cosmetic products, a limited number of 3D printer which is especially suitable for the production (in which cosmetics quality pigment and carrier mixture are used) of powdered cosmetics (eye shadow, blusher, face powder etc) to meet personal preferences in make-up products have been launched to markets.The first 3D printer was developed by Grace Choi in 2014 as a device to produce colored make-up products(Yapar, 2016).

Different molecular biological characteristics and diseases of patients show the importance of personalized forms of drugs in reaching success on the treatment of various diseases especially cancer. While there are common approaches for drugs and patients at the center of conventional clinical trials, there is a need for an approach centralizingpatient and patient-specific treatment, especially in the treatment of cancer. The current point in the concept of customized medicine according to the needs of patient is the use of three-dimensional/3D printing, that is,3D printer technology.This technology allows drugs to be prepared in safer and more effective dosage forms by designing their dose, size, appearance and release characteristicsaccording to the individual needs.Spritam®, the epilepsy preparation containing active ingredient levetiracetam produced by 3D printer, was the first drug approved by the US Food and Drug Agency in August 2015. These tablets prepared with a 3D printer, are dosage forms that are more readily soluble in contact with liquid than conventional tablets, easily ingested even at high dose contents, and with high dosage accuracy. Other advantages of dosage form production with 3D printing include pyramid-shaped tablets that can be used to allow the release of the active substance more rapidly than the cylindrical forms, dose adjustment to the microgram level and cost-effective production (Çağan and Yapar, 2018, Sastry et al., 2000, Uddin S, 2017, Ursan et al., 2013).

Apart from the advantages mentioned above, preparing 3D model which requires imaging and data processing has emerged as a time consuming effort rather than printing itself and the most healthcare personnel don't have this specific skill. Thus, total time necessary for 3D printing technology can do away with its advantages.

3D PRINTING METHODS AND APPLICATIONS

3D printing is a manufacturing method in which objects are made by fusing or depositing materials such as plastic, metal, ceramics, powders, liquids, or even living cells in layers to produce a 3D object. Some 3D printers are similar to traditional inkjet printers;

however, the product differs in that a 3D object is produced. 3D printing methods can be divided in five technics as the following(Ventola, 2014);

1. Stereolithography (SLA): The first commercial version SLA-250. A process based on curing of photoresin(epoxy or acrylic resin) layers by UV triggering.
2. Thermal Inkjet (Inkjet Printing): A process based on powder-liquid bonding using the polyjet technology of photoresins or, more often, of plaster powder (hybrid between SLA and Inkjet).
3. Selective Laser Sintering (SLS): Amethod based on heating powder PC, PVC, ABS, nylon, resin, polyester, metals, ceramic powder by laser triggering.
4. Fused Deposition Modeling (FDM): A technique based on shaping melted thermoplastics such as wax blends, PC, PS, ABS, nylon, metals / ceramics (with binder).
5. Laminated Object Manufacturing (LOM): A method based on cutting the sheets of adhesive coated polymers, papers, cellulose, metals with laser or razor.

Application in Biomedical Field

Surgical Planning

Surgeons can perform operations with better outcomes by planning via 3D printed models of human specimens such as brain and heart. Although the complexity of the nature of these organs, prototyping technology with 3D printing improves the understanding and conceptualization of the anatomy before operation compared to 3D simulated models on screen. The study with 3D printed models being done for defects is also more efficient enabling various approaches and hands-on experience. Due to the possible contributions to shorter and successful operations, 3D printing technology has been widely used in this application.

Prostheses

Patient-specific prostheses of hands, arms, feet and legs can be cost efficiently printed by anyone at anywhere. This high accessibility and affordability makes 3D printed prostheses essential for people especially children with missing or damaged limbs so as to keep on their normal life. In proper model and dimensions, both functional and aesthetically pleasing 3D printed prostheses are fully customizable with high precision to the wearer. However, as metal usage in 3D printing is not so common, they are generally lack of long term durability.

Medical Education and Training

Realistic 3D printed anatomical models which can be customized for any clinical scenario reduce many apprenticeship observations of medical students and help gaining required memorable skills in shorter time. In addition to their ability to be copied many times

with different sizes, damage-free transportation and handling during procedures is also possible and they can be thought as an alternate for high cost cadaver.3D printed tissue mimicking materials are durable to withstand punctures facilitating medical practice. Thus, they have promising utility in the assessment of interventional radiology.

Medical research

The drug response depending on in vitro or in vivo animal platforms varies and is different than that in human body. As one of the solutions to this problem,the usage of biomaterials or cells in 3D printing is possible and has allowed tissues to be reproducibly made. These tissues containing multiple types of cells represent the microenvironment needed to get a suitable response for a drug. Therefore, 3D printing technology for testing purposes to understand drug metabolism and toxicity is so attractive. Because of importance on toxicity, vasularized liver tissues have been commonly created which may open the doors of individual drug screening.Furthemore, researchers exploit 3D printed synthetic tumors to investigate disease profile.

Organ Printing

One of the main causes of the deaths in many countries is thelacking of transplant tissues. Organs which can be 3D printed and function have potential to be used as replacement. With lower biochemical reactions happening compared to liver and kidneys, fully functional 3D printed heart is the most possible. In this way, the first 3D printed heart with necessary blood cells, ventricles and chambers has been managed to produce by using cells and biological materials from a patient in Tel Aviv University(Noor et al., 2019). Although vascularization problems, that is, difficulty for forming the smallest vessels, that they can be implantable in human is not far away with developing research technology.

Application in Pharmaceutical Field

Drug Dosage and Delivery

3D printing method presents the opportunity for fabrication of tablets with different microstructures in which more than one active ingredient exist. Unlike conventional tablets which break unequally and lose its mass after splitting, the precise control over the geometry and amount of these ingredients can lead to the tablets with intended dissolution profiles based on the patient. Focusing on the patient-centric drug product development, the release profiles of chlorpheniramine and acetaminophen tablets were modified(Yu et al., 2009, Rowe et at., 2000). By means of 3D printing technology, dosage form adjustment according to the patient’s body weight and lifestyle has been also applied to multifunctional drug delivery systems. 3D printing is promising for individually developed dosage forms and drug delivery systems but operable dosage form formulation on the industry needs to be investigated with further research.

Application in Cosmetics Field

Due to the application of cosmetics to the human body, the use of 3D printer technology in the cosmetic field which health authorities play active role is quite new. The use of 3D printing technology in the cosmetic field has begun with the use of three-dimensional human skin models in effectiveness studies. It is known that 100,000 tissue samples of 0.5 cm^2 size are produced from skin samples donated by plastic surgery patients.

Home-type first 3D printer in the market by which especially colorful make-up products (eye shadow, eyebrows, blush, powder, etc.) can be produced according to personal preferences in the cosmetic field is seen as the most important development. In May 2014, Grace Choi presented his invention called "Mink"in the US for the first time for the home-type production of colored make-up products with 3D printer and designed it as a practical production method which can be performed at home according to especially the personal color preferences. Mink is a desktop printer that prints makeup by mixing of pigment and carrier material. Choi's motto for 3D production of cosmetics was "DIY Cosmetics". 3D printing is createdwith Mink by processing FDA-approved ink (cosmetic quality pigment and carrier mixture) on the printer for a color that can be selected from the Internet (businessinsider, 2019, intothegloss, 2019).

The use of 3D Printer Technology, which is also used in the field of packaging, in the production of Cosmetic Packaging is an important development for the cosmetics industry. Packaging design and visuality in cosmetics industry is an important parameter in terms of creating a demand. In 2013, Collcap Packing in the UK began to produce perfumes and other cosmetic packaging with Stratasys Objet30 Pro 3D printer. With seven different material options, they started to produce high-temperature packaging with transparent-to-mat, in colors ranging from blue, gray, white and black. While transparent material is an alternative to glass and PMMA, the cosmetic manufacturers are allowed to produce the packaging samples which can be designed and presented in a short time with the 3D Printer and there exists multiple alternatives in the selection and easy production of them (blog.stratasys, 2019).

CONCLUSION

As a result, it is expected that 3D printer technology, which is one of the current applications of technological developments and inventions that bring design and manufacture together, will progress rapidly, diversify and grow and that these will have critical reflections on the pharmaceutical industry.

REFERENCES

Ashraf H, Meer B, Naz R, Saeed A, Sadia H, Sajid U, Nisar K, Aslam Z, Anwar P. 3D-Bioprinting: A stepping stone towards enhanced medical approaches. Adv Life Sci, 2018; 5(4): 143-153.

Çağan B, Yapar EA. Biotechnological Drugs for Cancer Treatment and Clinical Trials. International İVEK Biotechnology Congress, 26-28 November 2018, Ottoman Archives Meeting Halls, İstanbul, Turkey.

Gross BC, Erkal JL, Lockwood SY, Chen C, Spence DM. Evaluation of 3D printing and its potential impact on biotechnology and the chemical sciences. Analytical Chemistry, 2014; 86(7):3240-3253.

Kandárová H, Hayden P, Klausner M, Kubilus J, Kearney P, Sheasgreen J. In vitro skin irritation testing: improving the sensitivity of the EpiDerm skin irritation test protocol. ATLA-Alternatives to Laboratory Animals, 2009; 37(6): 671.

Karagöl B. 3D Printing: What does it offer and for whom? METU TEKPOL Working Paper Series STPS-WP-15/02, 2015.

Noor N, Shapira A, Edri R, Gal I, Wertheim L, Dvir T. 3D Printing of Personalized Thick and Perfusable Cardiac Patches and Hearts, Advanced Science, 2019; 1900344.

Paul GM, Rezaienia A, Wen P, Condoor S, Parkar N, King W, Korakianitis T. Medical Applications for 3D Printing: Recent Developments. Missouri Medicine, 2018; 115(1): 75-81.

Rowe C, Katstra W, Palazzolo R, Giritlioglu B, and Teung P. Multi Mechanism Oral Dosage Forms Fabricated by Three Dimensional, Journal of Controlled Release, 2000; 66: 11-17.
Sastry SV, Nyshadham JR, Fix JA.Recent technological advances in oral drug delivery - a review. Pharm SciTechnolo Today, 2000; 3(4): 138-145.

Uddin S. 2017. Quality Control of Pharmaceuticals: Compendial Standards and Specifications.Scholars' Press, 10-140.

Ursan ID, Chiu L, Pierce AJ. Three-dimensional drug printing: a structured review Am Pharm Assoc, 2013; 53(2): 136-144.

Ventola CL, Medical Applications for 3D Printing: Current and Projected Uses. P T, 2014; 39(10): 704–711.

Yapar EA. Manufacturing by 3D Printing in Personal Care Products Industry. 3rd International Cleaning and Personal Care Products and Production Technologies Symposium and Exhibition. UCTEA Chamber of Chemical Engineers, 3-5 November 2016, İzmir, Turkey.

Yu DG, Branford-White C, Yang YC, Zhu LM and Welbeck EW. A Novel Fast Disintegrating Tablet Fabricated by Three-dimensional printing, Drug Development and Industrial Pharmacy 2009; 35: 1530-1536.

Available at: http://www.businessinsider.com/how-to-3d-print-lipstick-makeup-eyeshadow-and-nail-polish-from-a-home-computer-2014-9. [Accessed 11 May 2019].

Available at: https://intothegloss.com/2015/05/3d-printing-makeup/. [Accessed 11 May 2019].

Available at: http://blog.stratasys.com/2013/03/21/collcap-3d-printed-perfume-cosmetic-packaging/. [Accessed 11 May 2019]