

## Review Article

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## A Review On 3d Printed Tablets : A Downloadable Medicine

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### ABSTRACT

3Dimensional (3D)-printing is a rapid prototyping or additive manufacturing is a recent innovative technology that manufacture 3D shapes in a layer by layer method directly by computer aided drug design technology. Computer aided drug design(CADD) is an emerging tool for research and drug development process as it reduce the time taken for the process of drug development and expense. In 3D printing successive layers of material are formed under computer control to create an object. It is having high degree of flexibility over controls over the release of drug which is formulated as in different layers of tablets. 3D printing has an exclusive opportunity for the preparation of personalized medication to patient needs. This review deals with the scope of the 3D printing technology, various methods of preparation and regulatory problems with 3D printing pharmaceuticals.

**Key-words:** Computer aided drug design, 3D printing, personalized medication, and regulatory problems.

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### Introduction:

3D printing also known as additive manufacturing refers to a various processes used to synthesize a three dimensional object. In 3D printing successive layers of material are formed under computer control to create an object<sup>1</sup>. 3D printing was used as a novel medicine formulation technique for production of viable tablets capable of satisfying regulatory tests and matching the release of standard commercial tablets<sup>2</sup>.

Early additive manufacturing equipment and materials were developed in the 1980's. Hideo Kodama of Nagoya Municipal industrial Research institute invented to AM fabricating methods of 3D plastic model with photo Harding polymer, where the UV exposure area is controlled by a mask pattern or scanning fiber transmitter. In 1984, Check Hull of 3D systems corporation developed a prototype systems based on a process as a systems based on a process known as Stereolithography. The Umbrella term additive manufacturing gained wider currency in the decade of the 2000's<sup>1</sup>.

The need to formulate drugs that have narrow therapeutic indices like immunosuppressant's, blood thinners etc... the increase of proteomic and metabolomic analyses and the concomitant development of drugs & drugs combination to the patients are powerful drivers shaping the future of medicine design. Some patients require medications that are faster acting, while others need medications to be released more gradually over a longer period of time, 3D printing offers one the ability to customize medications for individual patient needs.

The vision behind 3D printing is that medication will be customized to individuals in that make it safer and more effective. The size, dose, appearance and rate of delivery of a drug can be designed to suit an individual<sup>3</sup>. Some patients require medications that are faster acting, while others need medications to be released more gradually over a longer period of time, 3D printing offers one the ability to customize medications for individual patient needs. The capability for dispensing low volumes with accuracy, specific spatial control and layer by layer assembly allow for the preparation of complex compositions and geometry. The high degree of flexibility and control with 3D printing allows preparation of dosage forms with multiple layers of active ingredients<sup>4</sup>.

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### Techniques involved:

A large number of additive processes are now available. The main differences between processes are in the way layers are deposited to create parts and in the materials that are used. They are mainly classified as

1. Stereo lithography
2. Selective laser sintering (SLS)
3. Multi- jet modeling (MJM)
4. Inkjet 3D printing

Computer aided drug design(CADD) is an emerging tool for research and drug development process as it reduce the time taken for the process of drug development and expense. Several new technologies have been developed and applied in drug R & D to shorten the research cycle and to reduce the expenses. In computer aided drug design process so many computational tools are used such as over viewing tools, homology modeling, and homology modeling programs, molecular dynamics, molecular docking and QSAR descriptors. This article provides a brief idea on computer aided drug design process and list of software used. For the modeling of the tablet shapes we are using solid CAD. Different purposes need different software's.

1. *Stereo lithography*: These are tank with photosensitive resin and ultraviolet source (a laser) to trace out the design of a model that have been uploaded to the machine. A print platform is lowered into the resin pool and the laser strikes the pool of resin from underneath, hardening the resin as it draws out the pattern layer by layer<sup>6</sup>.
2. *Selective laser sintering (SLS)*: SLS also uses a focused laser beam, but to sinter areas of a loosely compacted plastic, powder, the powder being applied layer by layer. In this method, a thin layer of powder is spread evenly onto a flat surface with a roller mechanism. The powder is then raster- scanned with a high power laser beam, the powder material that is struck by the laser beam is fused, while the other areas of powder remain dissociated. Successive layers of powder are deposited and raster scanned, one on top of another, until an entire part is complete. Each layer is sintered deeply enough to bond it to the preceding layer.

3. *Multi-jet modeling (MJM)*: This again builds up objects from successive layers of powder, with an inkjet-like print head used to spray on a binder solution that glues only the required granules together. The V-Flash printer, manufactured by Canon, is low-cost 3D printer. It's known to build layers with a light-curable film. Unlike other printers, the VFlash builds its parts from the top to down.
4. *Inkjet 3D printing*: In this method the material being jetted and acts as a binder, and is selectively sprayed into a powder bed of the part material to fuse it a layer at a time to create or print the required part. As it the case with other powder bed systems, once a layer is completed, the powder bed drops increases gradually and a roller smoothes the powder over the surface, before it pass to the jet hands, with the binder for the subsequent layer to be formed and fused with previous layer<sup>7</sup>.

Unlike other process, these techniques are optimized for speed, low cost and ease of use. No toxic chemicals like those used in stereo lithography are required. After printing the finished work takes place with in less time. Allows overhangs and excess powder can be easily removed with an air blower. These are advantages for this technique compare with others.

Photopolymerizable biocompatible water soluble polymers include polyethylene glycol tetraacrylate which can be photopolymerized with an argon laser under biologically compatible conditions using an initiator such as triethndamine, N-vinylpyrollidone and eosin-Y. The key benefit of 3D printing of tablet is to develop the personalized medication to the individual.

#### **Personalized medication:**

The vision behind 3D printing is that medication will be customized to individual in way that makes it safer and more effective. The size, dose, appearance and rate of delivery of a drug can be designed to suit an individual<sup>8</sup>. 3D printing has enabled the creation of high dose rapid dissipation pills, affording doctor reliable customization and complete control over the speed and strength of delivered dosage.

The term "personalized medicine" is often described as providing "the right patient with the right drug at the right dose at the right time. More broadly, personalized medicine (also known as precision medicine) may be thought of as the tailoring of medical treatment to the individual characteristics, needs, and preferences of a patient during all stages of care, including prevention, diagnosis, treatment, and follow-up. The drugs and treatments we devise are tested on broad populations and are prescribed using statistical averages. Consequently, they work for some patients but not for many others, due to genetic differences among the population. An average, any given prescription drug now on the market it works only for half of those who take it. Personalized medicine, because it is based on each patient's unique genetic makeup, is beginning to overcome the limitations of traditional medicine. This breakthrough technology, could also allow manufactures to shift their production and distribution process closer to consumers hospitals and pharmacies could manufacture prescription on their own premises<sup>8</sup>.

#### **Recent innovations:**

The FDA proves the first 3D printed pill to help to prevent epileptic seizures. The 3D printed LEVETIRACETAM pill was approved for use by US FDA this past august by the trade name of SPRITAM® and expected to be available soon in 2016. SPRITAM utilizes Aprecia's proprietary Zip Dose® Technology platform, a groundbreaking advance that uses three-dimensional printing (3DP) to produce a porous formulation that rapidly disintegrates with a sip of liquid. While 3DP has been used previously to manufacture medical devices, this approval marks the first time a drug product manufactured with this technology has been approved by the FDA<sup>9</sup>.

Zip dose creates pills that instantly dissolve on the tongue with a sip of liquid a potential born to those who have trouble swallowing traditional medication<sup>10</sup>.



Figure 1: 3D printed tablets<sup>21</sup>

### Research study:

The most recent study in favor of 3D printed pills comes from North Carolinian's wake forest university, where research developed a computer algorithm to design and calculate dosage according to patients instead of using predetermined dosages. S.A.Khaled et al; has done an experiment on desktop 3D printing of controlled release bilayer tablets of Guaifenesin by using HPM C 2910 as a binder solution. J.S.Park, H.J.Lee studied the 3D printing controlled release tablets of Dexibuprofen hydrogel composed of poly-lactic acid as a 3D printing material. Alvaro Goyanes have recently published an article about feasibility of combining hot melt extrusion with 3D printing technology on 4% paracetamol loaded filaments of polyvinyl alcohol<sup>11</sup>.

There are different shapes and sizes of 3D tablets are available. The drug release from the tablet is depends on the geometrical shape of the tablet.

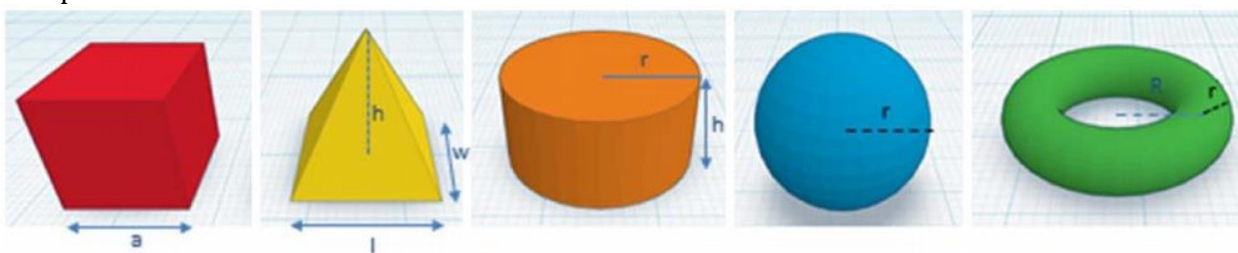


Figure 2: different shapes and sizes of 3d printed tablets

It turns out that the surface area-to-volume ratio is an important property and determinant in kinetics of drug release. A pyramid and standard cylinder are not created equal—with the pyramid able to deliver drug more expediently based on kinetic studies. The take-away point is that the one-size-fits-all approach is not optimal for patients who require continuous adjustments in their dosage.

### Quality control of 3D tablets:

Mass manufactured tablets are regulated and tested. 3D printed tablets are also needed quality control test like as now we are doing for the traditional tablets<sup>12</sup>. Pharmaceutical society's Jayne Lawrence says that It' likely a pharmacist would print tablets as they are sanctioned to make medicines. But before we get to that stage, 3d printed tablets will have to be systematically testes to make sure they are safe and work properly. Quality control test include dissolution, content uniformity and hyper spectral imaging is for NIR hyper spectral images were acquired for the samples using hyperspectral chemical imaging workstation sisu CHEMA which utilizes a specim MCT based spectral camera<sup>13</sup>.

Niklas Sandler<sup>14</sup> is investigating hyperspectral imaging used to of edifice quality control into printing drugs. Alhnan speculates that it may add up to regulate the finished, printed product but suggests that printed medicines would also need to be manufactured under the supervision of someone with a license to operate 3D printer and dispense drugs. License is granted by the regulatory bodies it must be validated before every use of equipment to check will printers give same product each time<sup>15</sup>.

Hyperspectral image technique takes thousands of spectral images at one time across an entire sample with each spectrum becoming a pixel in an overall image of what the sample contains, chemically at each point. 3D printer operators give assurance to regulatory authority that the printed tablets contains drug which was mentioned on

the label. There is a lot of regulation in medicine. This technology could be used more quickly for less potentially harmful tablets, like vitamins and supplements.

### Advantages and Disadvantages

- By altering the pills surface area; we can control the strength of a released dose as well as the time over which it's released. Research has found that the rate of drug release is dependent not on surface area, but on the surface area-to-volume ratio<sup>16</sup>.
- This process means we can produce tablets much closer to the patient." By making slight adjustments to the software before printing, hospitals could adjust doses for individual patients, a process of personalization that is otherwise prohibitively expensive<sup>17</sup>.
- Able to produce various shapes of the tablet. Other than routinely used in traditional methods.
- Small batches can be produced based on individual preferences<sup>18</sup>.

### Future medication

Medication printing technology could revolution the pharmaceutical industry, making drug research, development and production considerably cheaper. This could make it more cost effective for pharmaceuticals companies to safety drugs for rare diseases<sup>19</sup>.

The chances are that high street pharmacists will be able to tailor and print out customized drugs within the next decade<sup>20</sup>. 3D printing technology is already up and running in many areas. It is predicted by some additive manufacturing recommended that this technology development will change the nature of commerce, because end users will be able to do much of their own manufacturing rather than engaging in trade to buy products from the manufacturing companies<sup>21</sup>.

We may never do away with the need for the corner pharmacy to fill prescription, but 3D printers could fundamentally change the way patients take certain types of medicine. 3D printers could make possible a world of trade medicine in which patients take their own medicine.

### Conclusion

Nothing communicates ideas faster than a three-dimensional design .3D printed tablet is a novel medicine which satisfies the multiple needs means one pill to satisfy them all by allowing the medication to be packaged in precise dosages with desired shapes and points to future of personalized medicine. In near future the pharmaceutical industries take the step for innovative manufacturing for highly personalized medication and patient health care.

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