3D-Printed Drug Delivery and Applications for Improved Patient Compliance

Introduction

While 3D printing drug delivery is still considered a novelty, health care providers deeply entrenched in patient care realize the potential for greater therapeutic outcomes. Spritam as of 2016 is the only available medication of its kind, just receiving its FDA approval this past August thanks to manufacturer, Aprecia Pharmaceuticals. Similar to other formulations of Levetiracetam, it is approved to treat partial seizures in patients 4 years and older with epilepsy, myoclonic seizures in patients older than 12 years old with juvenile myoclonic epilepsy, and primary generalized tonic clonic seizures in patients older than 6 years presenting with idiopathic generalized seizures [1]. This breakthrough technology will allow for large dosing of medication that has the benefit of being fast melting, thereby providing a new option for patients struggling to swallow [2].

Although Spritam is the only FDA approved drug form of its kind, there have been other therapies experimenting with implementing various 3D methods. A 3D printed hydrophilic matrix Guaifenesin has been studied against the commercially available forms of Guaifenesin proving superior drug ferocity through the matrix [3,4]. Three near zero-order controlled release pseudoephedrine formulations were tested in a pharmacokinetic study in 10 healthy patients. Each of the pseudoephedrine compounds exhibited different release rates implicating flexible therapy options for specialized patient populations [3,5]. Presently experiments with three active medications in one tablet have been initiated. A nifedipine, captopril, and glipizide formulation was synthesized into one medication and through 3D printing, optimal release of all three drugs was observed [3,6].

Methods

3D printing refers to a manufacturing technique known as additive manufacturing in order to construct 3D models layer by layer, a principle that lead to the discovery of Zip Dose technology and eventually, the highly porous Spritam. Formation of a fully functional Zip Dose begins with mixing a powder blend to make the first layer. After uniformity is ensured, a binding fluid is precisely deposited on top, adhering it to the next layer. This process repeated several times resulting in a highly porous, orodispersible medication. When introduced to infinitesimal traces of water, the bond between the powder and the aqueous fluid deteriorates and disintegration occurs on average in 11 seconds, depending on the components of the target drug [1] (Figure 1).

Improving Adherence

In the case of Levetiracetam, this method allows for a high loading dose up to 1000 mg with taste masking capabilities and ease of swallowing for compliance-limited populations, i.e. the elderly and children. The precise form of final intake also offers different options for those who require it - the dose can be taken orally followed by a glass of water or as a suspension created by mixing the tablet in water. Added versatility such as this creates another benefit whose utility may go unnoticed in patient care. Specifically, the suspension dose assures uniform delivery while mitigating the pill burden for those who have difficulty swallowing and managing their polypharmacy. Therefore, from a clinical standpoint it appears the use of Zip Dose technology may prove most impactful in patient groups prone to experiencing severe obstacles to adherence. With Levetiracetam patients, that obstacle often involves the shame and anguish of seizures, which can make adhering to a strict neurological regimen intractable. In a separate survey conducted in epilepsy patients (N=661), adherence issues were shown to have the potential to undermine treatment outcomes, with results indicating that as many as 45 percent of epilepsy patients reported experiencing a seizure after missing a dose of their medication [7]. In this regard, perhaps epilepsy patients are those best suited to assess the viability of a 3D printed drugs in practice.

Conclusion

Subsequent to the drug’s market approval, it was not immediately clear how it would benefit the mainstream population; however, with the advent of the drugs unique chemical properties, it has the potential to impact adherence in all manners positive. A route to accomplishing this feat begins with future studies of the dosage form involving therapeutic drug monitoring with the drug plasma levels as surrogates for adherence. Conversely if this proves to be ineffective in the epileptic population, ideally 3D printing may have a platform in Oncotherapy as scientists can reconcile medications to the patient’s intricate regimen.
References