

CLAIMS

What is claimed is:

Claim 1: A method for three-dimensional printing of an oral drug dosage form formulated and configured to provide a desired drug release profile, wherein the drug dosage form comprises a multi-layered structure comprising a plurality of layers of a first erodible material admixed with a drug having a pre-determined drug mass fraction (m_F), wherein the first erodible material is embedded in a second material not admixed with the drug, the method comprising:

- (a) dividing the desired drug release profile into a plurality of time intervals (t_n), each time interval corresponding to a layer in the multi-layered structure;
- (b) calculating the percentage of drugs to be released during each time interval ($\%L$);
- (c) calculating the thickness of each layer (H_n) of the multi-layered structure based on the erosion rate of the first erodible material (V), wherein $H_n = t_n * V$;
- (d) calculating the surface area of each layer based on $\%L$, H_n , m_F , total amount of drug in the oral drug dosage form (m_{DTot}), and the density of the first erodible material (ρ), wherein:

$$S_n = \frac{\%L * m_{DTot}}{\rho * H_n * m_F};$$

- (e) dispensing the first erodible material admixed with the drug based on the determined H_n and S_n for each layer, thereby printing the multi-layered structure;
- (f) before, after, or during step (e), dispensing the second material not admixed with the drug.

Claim 2: The method of claim 1, further comprising dispensing a top erodible material not admixed with the drug on top of the multi-layered structure to form a top layer, wherein the surface area of the top layer is the same or larger than the first layer of the multi-layered structure immediately underneath the top layer.

Claim 3: The method of claim 2, wherein the thickness of the top layer is determined based on the delay time needed for the drug release from the multi-layered structure.

Claim 4: The method of claim 2, wherein the top erodible material is the same as the first erodible material.

Claim 5: The method of claim 2, wherein the top erodible material is different from the first erodible material.

Claim 6: The method of claim 1, wherein the second material is erodible.

Claim 7: The method of claim 6, wherein the first erodible material and the second material have the same erosion rate.

Claim 8: The method of claim 1, wherein the second material is an insulating material that is impermeable to bodily fluid, wherein the insulating material forms a barrier between the bodily fluid and at least a portion of the multi-layered structure.

Claim 9: The method of claim 1, further comprising dispensing an insulating material that is impermeable to bodily fluid, wherein the insulating material forms a barrier between the bodily fluid and at least a portion of the multi-layered structure.

Claim 10: The method of claim 1, further comprising dispensing an intermediate material not admixed with the drug, wherein the intermediate material forms one or more intermediate layers between two or more layers of the first erodible material.

Claim 11: The method of claim 10, wherein the intermediate material is the same as the first erodible material.

Claim 12: The method of claim 10, wherein the intermediate layer is different from the first erodible material.

Claim 13: The method of claim 1, wherein the three-dimensional printing is carried out by fused deposition modeling (FDM).

Claim 14: The method of claim 13, wherein the FDM is non-filament FDM.

Claim 15: The method of claim 1, wherein the first erodible material and the second material are printed by different printing heads.

Claim 16: The method of claim 1, wherein the first erodible material and the top erodible material are printed by different printing heads.

Claim 17: The method of claim 1, wherein the first erodible material, the second erodible material, and the insulating material are printed by a different printing heads.

Claim 18: The method of claim 1, further comprising:

- i) determining the drug release profile of the oral drug dosage form produced by the method of claim 1;
- ii) comparing the drug release profile of the oral drug dosage form with the desired drug release profile;
- iii) adjusting one or more parameters selected from: the first erodible material, the second material, the surface area of the one or more of the layers of the first erodible material, the thickness of one or more layers of the first erodible material, and the mass fraction of the drug in one or more layers of the first erodible material; and
- iv) three-dimensional printing of a second oral drug dosage form based on the adjusted parameters.

Claim 19: The method of claim 1, wherein the release profile of the oral drug dosage form or second drug oral dosage form is equivalent to the desired release profile based on Chow's method or similarity factor calculation method.

Claim 20: The method of claim 1, further comprising creating a virtual image of the drug dosage form prior to the dispensing steps.

Claim 21: The method of claim 1, further comprising creating a computer model that contains the pre-determined parameters prior to the dispensing step.

Claim 22: The method of claim 1, further comprising feeding the pre-determined parameters to the three-dimensional printer prior to the dispensing step.

Claim 23: The method of claim 1, wherein the surface area of each of the plurality of the layers of the first erodible material in the multi-layered structure decreases sequentially from the surface to the interior of the oral dosage form, wherein when the oral dosage form is exposed to a bodily fluid the plurality of layers are exposed to the bodily fluid in a sequential pattern, with the layer with the largest surface area exposed to the bodily fluid first.

Claim 24: The method of claim 1, wherein the oral drug dosage form comprises two or more multi-layered structures.

Claim 25: A method for three-dimensional printing of an oral drug dosage form formulated and configured to provide a first desired drug release profile and a second desired drug release profile, wherein the drug dosage form comprises a first multi-layered structure comprising a plurality of layers of a first erodible material admixed with a drug having a pre-determined drug mass fraction (m_F), wherein the first erodible material is embedded in a second material not admixed with a first drug, and a second multi-layered structure comprising a plurality of layers of a third erodible material admixed with a fourth drug having a pre-determined drug mass fraction, wherein the third erodible material is embedded in a fourth material not admixed with the drug,
the method comprising:

- (a) dividing each of the desired drug release profile into a plurality of time intervals (t_n), each time interval corresponding to a layer in a corresponding multi-layered structure;
- (b) calculating the percentage of drugs to be released during each time interval ($\%L$);
- (c) calculating the thickness of each layer (H_n) of the multi-layered structures based on the erosion rate of the first erodible material or third erodible material (V), wherein $H_n = t_n * V$;
- (d) calculating the surface area of each layer based on $\%L$, H_n , m_F , total amount of drug in the oral drug dosage form ($m_{D\text{Tot}}$), and the density of the first or first erodible

material (ρ), wherein:

$$S_n = \frac{\%L * m_{DTot}}{\rho * H_n * m_F};$$

- (e) dispensing the first erodible material admixed with the first drug and third erodible material admixed with the second drug based on the determined H_n and S_n for each layer, thereby printing the two multi-layered structures;
- (f) before, after, or during step (e), dispensing the second material and fourth material not admixed with the drug.

Claim 26: The method of claim 25, wherein the first erodible material and the third erodible material are the same.

Claim 27: The method of claim 25, wherein the second and fourth materials are the same.

Claim 28: The method of claim 25, wherein the first drug and the second drug are the same.

Claim 29: The method of claim 25, wherein the first drug and the second drug are different.

Claim 30: An oral dosage form produced by the method of claim 1.