ORAL DRUG DOSAGE FORMS HAVING A DESIRED PK PROFILE AND METHODS OF DESIGNING AND PRODUCING THEREOF

TECHNICAL FIELD

[0001] The present disclosure, in some aspects, is directed to methods of designing an oral drug dosage form formulated and configured to have a desired pharmacokinetic profile. In other aspects, the present disclosure is directed to oral drug dosage forms having a desired pharmacokinetic profile, and methods of making, such as three-dimensional printing, such oral drug dosage forms.

BACKGROUND

[0002] The growing understanding of the mechanisms of drugs and reagents increasingly illustrates the importance of precision *in vivo* drug delivery to ensure optimized delivery in location, time, and amount, to achieve a desired pharmacokinetic profile for best use, efficacy, and safety of said drugs, drug candidates, and reagents. To achieve a desired pharmacokinetic profile, certain drugs and reagents may require, *e.g.*, complex release profiles and/or administration dosing regimen. However, such demands required often run counter to manufacturing constraints and ensuring proper use and patient compliance via simplicity of administration, *e.g.*, once-daily oral dosage forms or delivery systems. Additionally, the design of a drug dosage form capable of achieving a desired pharmacokinetic profile in an individual may not be readily obtained, even when based on such testing as *in vitro* release profile testing.

[0003] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

BRIEF SUMMARY

[0003a] In an aspect of the present disclosure, there is provided an oral drug dosage form comprising a fixed amount of a drug formulated and configured to have a desired composite pharmacokinetic (PK) profile, the oral drug dosage form having two dosage units stacked back-to-back, wherein each dosage unit comprises:

an immediate-release (IR) portion comprising the drug, the IR portion having an immediate-release profile; and/or

an extended release (ER) portion comprising the drug, the ER portion having an extended-release profile; and

a shell,

wherein the IR portion has a top surface and a bottom surface, wherein the ER portion has a top surface and a bottom surface, wherein the shell partially surrounds the IR portion and the ER portion, and wherein the shell is in direct contact with both the IR portion and the ER portion and leaves one surface of the IR portion or one surface of the ER portion exposed; the drug in the IR portion is the same as the drug in the ER portion; the dosage unit further comprises an intermediate layer which is not admixed with a drug, wherein the intermediate portion is positioned between the IR portion and ER portion; wherein the shell has a slower dissolution rate than the ER portion or the shell is non-erodible.

[0004] In some examples, the present disclosure provides a method of designing an oral drug dosage form having a fixed amount of a drug and a desired composite pharmacokinetic (PK) profile in an individual, wherein the oral drug dosage form comprises a dosage unit comprising: a first modulated-release (MR1) portion comprising the drug; and a second modulated-release (MR2) portion comprising the drug, the method comprising: (a) obtaining a MR1 PK curve of a MR1 precursor drug dosage form comprising the MR1 portion in the individual; (b) obtaining a MR2 PK

CLAIMS

1. An oral drug dosage form comprising a fixed amount of a drug formulated and configured to have a desired composite pharmacokinetic (PK) profile, the oral drug dosage form having two dosage units stacked back-to-back, wherein each dosage unit comprises:

    an immediate-release (IR) portion comprising the drug, the IR portion having an immediate-release profile; and / or

    an extended release (ER) portion comprising the drug, the ER portion having an extended-release profile; and

    a shell,

wherein the IR portion has a top surface and a bottom surface, wherein the ER portion has a top surface and a bottom surface, wherein the shell partially surrounds the IR portion and the ER portion, and wherein the shell is in direct contact with both the IR portion and the ER portion and leaves one surface of the IR portion or one surface of the ER portion exposed; the drug in the IR portion is the same as the drug in the ER portion; the dosage unit further comprises an intermediate layer which is not admixed with a drug, wherein the intermediate portion is positioned between the IR portion and ER portion; wherein the shell has a slower dissolution rate than the ER portion or the shell is non-erodible.

2. The oral drug dosage form of claim 1, wherein the drug has linear pharmacokinetics.

3. The oral drug dosage form of claim 1 or 2, wherein the IR portion and the ER portion are stacked on top of each other.

4. The oral drug dosage form of claim 1 or 2, wherein the IR portion and the ER portion are positioned side-by-side with each other.

5. The oral drug dosage form of claim 3, wherein, at least in one of the dosage units, the IR portion is stacked on top of the ER portion, and wherein the shell leaves only the top surface of the IR portion exposed.

6. The oral drug dosage form of claim 5, wherein the bottom surface of the IR portion is in direct contact with the top surface of the ER portion.

7. The oral drug dosage form of claim 5 or 6, wherein the dosage unit further comprises a second IR portion, wherein the second IR portion has a top surface and a bottom surface, wherein the ER portion is stacked on top of the second IR portion, and wherein the shell leaves only the top surface of the IR portion exposed.

8. The oral drug dosage form of claim 7, wherein the bottom surface of the ER portion is in direct contact with the top surface of the second IR portion.

9. The oral drug dosage form of claim 3, wherein, at least in one of the dosage units, the ER portion is stacked on top of the IR portion, and wherein the shell leaves only the top surface of the ER portion exposed.

10. The oral drug dosage form of claim 9, wherein the bottom surface of the ER portion is in direct contact with the top surface of the IR portion.

11. The oral drug dosage form of any one of claims 1-10, wherein the two dosage units are the same.

12. The oral drug dosage form of any one of claims 1-10, wherein the two dosage units are different.

13. The oral drug dosage form of any one of claims 1-12, wherein substantially all of the IR portion erodes within at least about 20 minutes after the oral drug dosage form is to be administered to an individual.

14. The oral drug dosage form of claim 13, wherein the IR portion comprises an erodible material.

15. The oral drug dosage form of any one of claims 1-14, wherein the ER portion comprises an erodible material, and wherein the drug contained in the ER portion is released from the oral drug dosage form over a period of at least about 6 hours.