controlled release theophylline pellet preparation and evaluates network performance by comparing the predicted dissolution profiles with those obtained from physical experiments using similarity factor.

[0008] Juliet Obianuju Njoku *et.al.* discloses a software based system for predicting excipient influence on dissolution profiles involving amorphous solid dispersion systems. The objective of this study is to assess formulation specific models in simulating drug-excipient interaction using DDDPlus, by determining the impact of prediction factors in the program on solubilizer and disintegrant effect on the dissolution profile of an immediate release, poorly soluble drug.

[0009] US 10,216,911 B2 discloses a method for predicting compound solubility, involving calculating a free energy of solubility for a compound in a solvent, where an initial state is established for a system by a computer model that contains an aggregate of multiple molecules.

[0010] WO 2020/016,579 A2 discloses a machine-learning based method of analyzing drug-like molecules, that involves representing molecular quantum states of each drug-like molecule as a quantum graph, and feeding that quantum graph as input to machine learning system

[0011] In view of foregoing disclosures, still there is a need to establish a reliable system for amorphous solid dispersion design, that helps to predict various properties of ASDs.

[0012] In the present invention, an artificial intelligence-based system is disclosed using both experimental results data and molecular simulation to predict various properties of ASDs. This system enables rational design of ASDs for poorly water-soluble drugs and may significantly reduce the time and resources required for ASD based formulation development.

SUMMARY

[0013] In a first aspect, the present disclosure provides a method of predicting properties of amorphous solid dispersions, the method comprising, at an electronic device having a processor: obtaining a machine learning model trained to predict a dissolution, thermophysical, or stability property of an amorphous solid dispersion based on at least one parameter of at least one first ingredient, wherein the machine learning model is trained based on comparing (a) a predicted dissolution, thermophysical, or stability property predicted based on the at least one first ingredient with (b) an experimentally-determined dissolution, thermophysical, or stability property that is

experimentally determined using the at least one first ingredient; determining at least one parameter of at least one

second ingredient of a second amorphous solid dispersion; and predicting at least one dissolution, thermophysical, or stability property of the second amorphous solid dispersion by inputting the at least one parameter of the at least one second ingredient to the machine learning model.

[0014] In some implementations, a machine learning model is trained to predict properties of amorphous solid dispersions by performing steps comprising: (i) creating a plurality of experimental results data of at least one first ingredient of an amorphous solid dispersion; (ii) generating molecular simulation properties of at least one first ingredient of the amorphous solid dispersion of step (i); (iii) implementing a machine learning model (e.g., an artificial neural network) using experimental results data of step (i) and molecular simulation properties of step (ii). The machine learning model is used to predict the properties of amorphous solid dispersions comprising at least one second ingredient. The machine learning model may be updated over time with additional training, e.g., based on new experimental result and/or molecular simulation data.

[0015] In another example, the ingredient of the amorphous solid dispersion is selected from the group consisting of polymers, drugs, sugars, sugar alcohols, surfactants, organic acids and bases, inorganic molecules, co-solvents, co-excipients, plasticizers, and combinations thereof.

[0016] In another example, the ingredient of the amorphous solid dispersion is selected from at least one drug and at least one polymer.

[0017] In another example, the predicted properties of the amorphous solid dispersions include glass transition temperature, physical stability, maximum drug concentration during dissolution in Fasted State Simulating Intestinal Fluid *[FaSSIF (C_{max})],* and drug concentration at 120 min during dissolution in Fasted State Simulating Intestinal Fluid *[FaSSIF (C_{120})].*

[0018] In a second aspect, the present disclosure provides a system for predicting properties of the amorphous solid dispersions comprising at least one computer system comprising (i) a memory configured to store at least one program, (ii) a processor, and (iii) a visualization interface, or combinations thereof, capable of executing the steps of: (i) receiving a plurality of experimental results data of at least one first ingredient of an amorphous solid dispersion; (ii) generating a plurality of two-dimensional or three-dimensional structures of at least one first ingredient of the amorphous solid dispersion of step (i); (iii) performing molecular simulation to generate molecular simulation properties of at least one first ingredient of the amorphous solid dispersion of step (ii);

(iv) implementing an artificial neural network using experimental results data of step (i) and molecular simulation

properties of step (iii); and (v) predicting the properties of amorphous solid dispersions comprising at least one second ingredient, using the artificial neural network of step (iv).

[0019] In another example, the computer system for predicting properties of the amorphous solid dispersions comprises (i) a memory configured to store at least one program, (ii) a processor (iii) a visualization interface, or combinations thereof.

[0020] In accordance with some implementations, a device includes one or more processors, a non-transitory memory, and one or more programs; the one or more programs are stored in the non-transitory memory and configured to be executed by the one or more processors and the one or more programs include instructions for performing or causing performance of any of the methods described herein. In accordance with some implementations, a non-transitory computer readable storage medium has stored therein instructions, which, when executed by one or more processors of a device, cause the device to perform or cause performance of any of the methods described herein. In accordance with some implementations, a device includes: one or more processors, a non-transitory memory, and means for performing or causing performance of any of the methods described herein.

BRIEF DESCRIPTION OF THE FIGURES

[0021] Further embodiments of the present application can be understood with reference to the appended figures.

[0022] **Figure 1** is a flow chart illustrating an exemplary process of predicting properties of amorphous solid dispersions using a trained artificial neural network.

[0023] **Figure 2a** illustrates a block diagram describing the process of implementing an artificial neural network.

[0024] **Figure 2b** illustrates a block diagram describing the process of predicting properties of amorphous solid dispersions using a trained artificial neural network.

[0025] **Figure 3** illustrates a graph representing actual versus predicted values of physical stability at 25 °C/60% relative humidity.

[0026] **Figure 4** illustrates a graph representing actual versus predicted values of physical stability at 40 °C/75% relative humidity.

What is claimed is:

1. A method of predicting properties of amorphous solid dispersions, the method comprising, at an electronic device having a processor:

obtaining a machine learning model trained to predict a dissolution, thermophysical, or stability property of an amorphous solid dispersion based on at least one parameter of at least one first ingredient, wherein the machine learning model is trained based on comparing (a) a predicted dissolution, thermophysical, or stability property predicted based on the at least one first ingredient with (b) an experimentally-determined dissolution, thermophysical, or stability property that is experimentally determined using the at least one first ingredient;

determining at least one parameter of at least one second ingredient of a second amorphous solid dispersion; and

predicting at least one dissolution, thermophysical, or stability property of the second amorphous solid dispersion by inputting the at least one parameter of the at least one second ingredient to the machine learning model.

2. The method according to claim 1, wherein the at least one parameter of the at least one first ingredient comprises at least one molecular simulation property.

3. The method according to claim 1, wherein said at least one parameter of the at least one second ingredient is an experimental active pharmaceutical ingredient (API) parameter, the experimental API parameter comprising a molecular weight, melting point, water solubility, or value associated with an experimental octanol water partition coefficient.

4. The method according to claim 1, wherein said at least one parameter of the at least one second ingredient is a computed active pharmaceutical ingredient (API) parameter, the computed API parameter comprising a number of hydrogen bond acceptors and donors, a solubility value, or a molecular volume, or said at least one parameter of the at least one second ingredient is a computed polymer parameter comprising a thermophysical property, a mechanical property, or a geometrical property.

5. The method according to claim 1, wherein the machine learning model is trained by:

(i) creating a plurality of experimental results data of the at least one first ingredient of at least one amorphous solid dispersions;

(ii) generating molecular simulation properties of the at least one first ingredient of the amorphous solid dispersion of step (i); and

(iii) training the machine learning model using experimental results data of step (i) and molecular simulation properties of step (ii), wherein said simulated properties preferably comprise density, solvation free energy, enthalpy of mixing, and solubility parameters.

6. The method according to claim 1, wherein said at least one first ingredient is selected from the group consisting of polymers, drugs, sugars, sugar alcohols, surfactants, organic acids and bases, inorganic molecules, co-solvents, co-excipients, plasticizers, and combinations thereof.

7. The method according to claim 6, wherein said polymer is selected from the group consisting of homo polymers, co-polymers, oligomers, ampholytic polymers, water soluble polymers, water insoluble polymers, ionizable polymers, non-ionizable polymers and combination thereof, or from the group consisting of synthetic polymers, natural polymers, nature derived polymers, semi-synthetic polymers, and combinations thereof, said synthetic polymer preferably being selected from the group consisting of polyvinylpyrrolidone homopolymer, poly(vinylpyrrolidone-*co*-vinyl acetate), crosslinked polyvinylpyrrolidone, polyvinyl caprolactam homopolymer, polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol copolymers, polyethylene glycol homopolymer, polyvinyl alcohol-polyethylene glycol co-polymers, ethylene oxide-propylene oxide co-polymers, ammonio methacrylate co-polymers, polyacrylic acid, polyacrylic acid co-polymers, polymethacrylic acid homopolymer, polymethacrylic acid co-polymers, polyvinylalcohol homopolymer, polyvinylalcohol co-polymers, polyvinyl acetate phthalate, n-methyl-2-pyrrolidone, bis-vinylcaprolactam, and combinations thereof, and said natural polymer and nature-derived polymer preferably being selected from the group consisting of cellulose, starch, chitosan, guar, methylcellulose, carboxymethyl cellulose, carboxymethyl cellulose acetate butyrate, ethyl cellulose, hydroxyethyl cellulose, methylhydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose acetate succinate, hydroxypropyl methylcellulose phthalate, cellulose acetate adipate, cellulose acetate adipate propionate, cellulose acetate phthalate, cellulose acetate suberate, cellulose acetate sebacate, 5-carboxypentyl hydroxypropyl cellulose, chitosan hydrochloride, hydroxypropyl-β-cyclodextrins, hydroxypropyl-γ-cyclodextrins, and combinations thereof.

8. The method according to claim 6, wherein said drug is selected from the group consisting of analgesic drugs, anti-inflammatory drugs, antiparasitic drugs, anti-arrhythmic drugs, anti-bacterial drugs, anti-viral drugs, anti-coagulant drugs, anti-cancer drugs, anti-depressant drugs, anti-diabetic drugs, anti-epileptic drugs, anti-fungal drugs, anti-gout drugs, anti-hypertensive drugs, antimalarial drugs, anti-migraine drugs, anti-muscarinic drugs, erectile dysfunction improvement drugs, immunosuppressant drugs, anti-protozoal drugs, anti-thyroid drugs, anxiolytic drugs, sedative drugs, hypnotic drugs, neuroleptic drugs, β-blocker drugs, cardiac inotropic drugs, antidiuretic drugs, anti-parkinson drugs, gastro-intestinal drugs, histamine receptor antagonists, lipid regulating drugs, anti-anginal drugs, Cox-2 inhibiting drugs, leukotriene inhibiting drugs, protease inhibitors, muscle relaxants, anti-osteoporosis drugs, anti-obesity drugs, cognition enhancing drugs, anti-urinary incontinence drugs, anti-benign prostate hypertrophy drugs, and combinations thereof, said sugar preferably being selected from the group consisting of mannitol, sorbitol, sucrose, maltose, soluble starches, α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, and combinations thereof, and said surfactant preferably being selected from the group consisting of anionic surfactants, cationic surfactants, nonionic surfactants, and combinations thereof.

9. The method according to claim 1, wherein said at least one first ingredient comprises at least one drug and at least one polymer.

10. The method according to claim 1, wherein said at least one dissolution, thermophysical, or stability property comprises glass transition temperature, physical stability of amorphous solid dispersions, maximum drug concentration during dissolution in Fasted State Simulating Intestinal Fluid [*FaSSIF* (C_{max})], or drug concentration at 120 min during dissolution in Fasted State Simulating Intestinal Fluid [*FaSSIF* (C_{120})], and preferably, said physical stability of amorphous solid dispersions is predicted employing at least two different temperatures and at least two relative humidity conditions.

11. A system for predicting properties of amorphous solid dispersions comprising at least one computer system comprising (i) a memory configured to store at least one program, (ii) a processor, and (iii) a visualization interface, or combinations thereof, capable of executing the steps of:

(i) receiving a plurality of experimental results data of at least one first ingredient of an amorphous solid dispersion;

(ii) generating a plurality of two-dimensional or three-dimensional structures of at least one first ingredient of the amorphous solid dispersion of step (i);

(iii) performing molecular simulation to generate molecular simulation properties of at least one first ingredient of the amorphous solid dispersion of step (ii);

(iv) implementing an artificial neural network using experimental results data of step (i) and molecular simulation properties of step (iii); and

(v) predicting the properties of amorphous solid dispersions comprising at least one second ingredient, using said artificial neural network of step (iv).

12. The system according to claim 11, wherein said second ingredient is different from said first ingredient of the amorphous solid dispersion, used for creating said experimental results data, said ingredient of the amorphous solid dispersion preferably being selected from the group consisting of polymers, drugs, sugars, sugar alcohols, surfactants, organic acids and bases, inorganic molecules, co-solvents, co-excipients, plasticizers, and combinations thereof.

13. The system according to claim 12, wherein said polymer is selected from the group consisting of homo polymers, co-polymers, oligomers, ampholytic polymers, water soluble polymers, water in-soluble polymers, ionizable polymers, non-ionizable polymers and combination thereof, or said polymer is selected from the group consisting of synthetic polymers, natural polymers, nature derived polymers, semi-synthetic polymers, and combinations thereof.

14. The system according to claim 13, wherein said synthetic polymer is selected from the group consisting of polyvinylpyrrolidone homopolymer, poly(vinylpyrrolidone-*co*-vinyl acetate), crosslinked polyvinylpyrrolidone, polyvinyl caprolactam homopolymer, polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol co-polymers, polyethylene glycol homopolymer, polyvinyl alcohol-polyethylene glycol co-polymers, ethylene oxide-propylene oxide co-polymers, ammonio methacrylate co-polymers, polyacrylic acid, polyacrylic acid copolymers, polymethacrylic acid homopolymer, polymethacrylic acid co-polymers, polyvinylalcohol homopolymer, polyvinylalcohol co-polymers, polyvinyl acetate phthalate, n-methyl-2-pyrrolidone, hydroxyethyl pyrrolidone, bis-vinylcaprolactam, and combinations thereof,

and/or said natural polymer or nature-derived polymer is selected from the group consisting of cellulose, starch, chitosan, guar, methylcellulose, carboxymethyl cellulose, carboxymethyl cellulose acetate butyrate, ethyl cellulose, hydroxyethyl cellulose, methylhydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose acetate succinate, hydroxypropyl methylcellulose phthalate, cellulose acetate adipate, cellulose acetate adipate propionate, cellulose acetate phthalate, cellulose acetate suberate, cellulose acetate sebacate, 5-carboxypentyl hydroxypropyl cellulose, chitosan hydrochloride, hydroxypropyl-β-cyclodextrins, hydroxypropyl-γ-cyclodextrins, and combinations thereof.

15. The system according to claim 12, wherein said drug is selected from the group consisting of analgesic drugs, anti-inflammatory drugs, antiparasitic drugs, anti-arrhythmic drugs, anti-bacterial drugs, anti-viral drugs, anti-coagulant drugs, anti-cancer drugs, anti-depressant drugs, anti-diabetic drugs, anti-epileptic drugs, anti-fungal drugs, anti-gout drugs, anti-hypertensive drugs, antimalarial drugs, anti-migraine drugs, anti-muscarinic drugs, erectile dysfunction improvement drugs, immunosuppressant drugs, anti-protozoal drugs, anti-thyroid drugs, anxiolytic drugs, sedative drugs, hypnotic drugs, neuroleptic drugs, β-blocker drugs, cardiac inotropic drugs, antidiuretic drugs, anti-parkinson drugs, gastro-intestinal drugs, histamine receptor antagonists, lipid regulating drugs, anti-anginal drugs, Cox-2 inhibiting drugs, leukotriene inhibiting drugs, protease inhibitors, muscle relaxants, anti-osteoporosis drugs, anti-obesity drugs, cognition enhancing drugs, anti-urinary incontinence drugs, anti-benign prostate hypertrophy drugs, and combinations thereof, and/or said sugar is selected from the group consisting of mannitol, sorbitol, sucrose, maltose, soluble starches, α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin and combinations thereof, and/or wherein said surfactant is selected from the group consisting of anionic surfactants, cationic surfactants, nonionic surfactants, and combinations thereof.

16. The system according to claim 11, wherein said ingredient of the amorphous solid dispersion comprises at least one drug and at least one polymer, and wherein said experimental results data comprise chemical structure, melting temperature, glass transition temperature of drug, dose, solubility, p*K*a, and octanol-water partition coefficient (log*P*).

17. The system according to claim 11, wherein said simulated properties comprise density, free energy, enthalpy of mixing, and solubility parameters.

18. The system according to claim 11, wherein said predicted properties comprise glass transition temperature, physical stability, maximum drug concentration during dissolution in Fasted State Simulating Intestinal Fluid [*FaSSIF (C_{max})*], and drug concentration at 120 min during dissolution in Fasted State Simulating Intestinal Fluid [*FaSSIF (C_{120})*].

19. The system according to claim 11, wherein said physical stability of amorphous solid dispersions is predicted employing at least two different temperatures and at least two relative humidity conditions.