IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Allen Greenspoon; Anthony Adili
Serial No.: 18/506,793
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Entitled: ORALLY ADMINISTRABLE FORMULATION

Confirmation No.: 9084
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Examiner:

THIRD-PARTY PRE-ISSUANCE SUBMISSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application.

1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021)
2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020)
3. U.S. Pat. App. Pub. No. US/2019/0192498 "Psilocybin composition" (Published June 27, 2019)

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. 18/506,793 Pending Claims	References
1. (Currently Amended) A formulation capable of being administered orally and being dissolved in the oral cavity, wherein said formulation comprises a hydrophilic polymer base comprising a hydrophilic elastomeric polymer in an amount of 50-80% by wt of the hydrophilic polymer base and a pharmaceutical component comprising one or more pharmaceutical agents and an enzymatic absorption enhancer in an amount of 0.01-10% by wt of the pharmaceutical component, wherein the hydrophilic polymer base and the pharmaceutical component are combined to form a non-micellar mixture.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."

2. (Currently Amended) The formulation of claim 1, wherein the hydrophilic polymer base comprises one or more hydrophilic elastomeric polymers selected from the group consisting of polyethylene glycol, polyacrylamides, polyacrylic acid, polyacrylic acid copolymer, polyvinyl alcohol, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinyl-pyrrolidone, carboxymethyl cellulose, polyglycolide, polylactide, methylmethacrylate copolymer, carboxyvinyl polymer, polysaccharides, and combinations thereof.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0019]** "The term **"plasticizer"** refers to a substance that, when added to polymer(s), they make the polymer more pliable and soft, enhancing the flexibility and plasticity of the films while reducing the brittleness. The plasticizer is believed to permeate the polymer structure, disrupting intermolecular hydrogen bonding, and permanently lowers intermolecular attractions. Plasticizers can be used to allow initial film forming, to reduce the brittleness, and improve the processability and flexibility of the resulting film, thereby avoiding cracking, e.g., during the curing process. Suitable plasticizers include, e.g., glycerin, water, **polyethylene glycol**, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof." From **[0023]** "The term "binder" refers to a substance, typically a polymer, used to hold the ingredients together. Binders ensure that the oral dissolvable films can be formed with the requisite mechanical strength. The binders also provide the requisite volume to low amount of active present in dissolvable films. The presence of the binder also facilitates the formation of the cured film. As such, the binder includes those substances, which when present in the cast slurry and upon curing, will effectively provide for a cured film. The binder may also be referred to as a "film forming agent," or more specifically a "film forming polymer" when it is a polymer. The polymer can be a natural polymer or a synthetic polymer. Natural polymers include, e.g., pullulan, sodium **alginate** (Na **alginate**), pectin, gelatin, chitosan, and maltodextrin. Synthetic polymers include, e.g., hydroxpropyl cellulose (HPC), hydroxpropyl methylcellulose (HPMC), **carboxymethyl cellulose** (CMC), sodium carboxymethylcellulose (CMC-Na), microcrystalline cellulose (MCC), **polyvinyl alcohol** (PVA), polyethylene oxide (PEO), polyvinylpyrrolidone (PVP), and Kollicoat® (e.g., Kollicoat® Protect or Kollicoat® IR)."

	From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, **polyacrylamides**, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
3. (Currently Amended) The formulation of claim 1, wherein the hydrophilic polymer base comprises a polysaccharide selected from the group consisting of pullulan, amylose, high amylose starch, hydroxypropylated high amylose starch, alginate, carrageenan, pectin, dextrin, dextran, chitin, chitosan, levan, elsinan, scleroglucan, and combinations thereof.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0023]** "The term "binder" refers to a substance, typically a

	polymer, used to hold the ingredients together. Binders ensure that the oral dissolvable films can be formed with the requisite mechanical strength. The binders also provide the requisite volume to low amount of active present in dissolvable films. The presence of the binder also facilitates the formation of the cured film. As such, the binder includes those substances, which when present in the cast slurry and upon curing, will effectively provide for a cured film. The binder may also be referred to as a "film forming agent," or more specifically a "film forming polymer" when it is a polymer. The polymer can be a natural polymer or a synthetic polymer. Natural polymers include, e.g., pullulan, sodium **alginate** (Na **alginate**), **pectin**, gelatin, **chitosan**, and **maltodextrin**. Synthetic polymers include, e.g., hydroxpropyl cellulose (HPC), hydroxpropyl methylcellulose (HPMC), carboxymethyl cellulose (CMC), sodium carboxymethylcellulose (CMC-Na), microcrystalline cellulose (MCC), polyvinyl alcohol (PVA), polyethylene oxide (PEO), polyvinylpyrrolidone (PVP), and Kollicoat® (e.g., Kollicoat® Protect or Kollicoat® IR)." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, **pullulan**, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone,

	diethylene glycol, castor oil, and combinations thereof."
4. (Currently Amended) The formulation of claim 1, wherein the hydrophilic polymer base additionally comprises a film-forming agent selected from the group consisting of xanthan gum, tragacanth gum, guar gum, acacia gum, carrageenan gum, collagen, gelatin, zein, gluten, soy protein isolate, whey protein isolate, casein, and mixtures thereof.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0024]** "The term "mucoadhesive agent" refers to a substance that, upon contact with a mucosal surface (e.g., oral cavity), will adhere therein. The mucoadhesive agent, when placed in the oral cavity in contact with the mucosa therein, will adhere to the mucosa. The mucoadhesive agent permits a close and extended contact of the composition of the oral dissolvable film with the mucosal surface of the subject, by promoting adherence of the composition to the mucosa, and facilitating the release of the active ingredient from the composition. The mucoadhesive agent can be a polymeric compound, such as a cellulose derivative but it can be also a natural gum, alginate, pectin, or such similar polymer. The concentration of the mucoadhesive agent can be adjusted to vary the length of time that the film adheres to the mucosa or to vary the adhesive forces generated between the film and mucosa. Mucoadhesive agents include, e.g., carboxymethyl cellulose (CMC), carboxymethyl cellulose sodium (CMC-Na), polyvinyl alcohol, polyvinyl pyrrolidone (povidone), sodium alginate, methyl cellulose, hydroxyl propyl cellulose, hydroxypropylmethyl cellulose, polyethylene glycols, carbopol, polycarbophil, carboxyvinyl copolymers, propylene glycol alginate, alginic acid, methyl methacrylate copolymers, **tragacanth gum**, **guar gum**, karaya gum, ethylene vinyl acetate, dimethylpolysiloxanes, polyoxyalkylene block copolymers, pectin, chitosan, carrageenan, **xanthan gum**, gellan gum, gum Arabic, locust bean gum, and hydroxyethylmethacrylate copolymers." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring

	agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, **gelatin**, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
5. (Currently Amended) The formulation of claim 1, wherein the absorption enhancer is an enzyme selected from the group consisting of pancreatic lipase, pancreatic lipase-related protein 1 or 2, hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase, and lingual lipase.	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme (cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited

	bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability."
6. (Original) The formulation of claim 1, wherein the absorption enhancer comprises an enzymatic absorption enhancer combined with a non-enzymatic absorption enhancer.	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) **From claim 9**. "The formulation of claim 5, wherein the detergent is selected from the group consisting of a **bile acid or a salt** thereof, and an aliphatic sulphate ester." From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme (cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability." 1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or

	gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0038**] "The term "antioxidant" refers to a substance that **inhibits or prevents oxidation** of any one of more substances present in the slurry and/or oral dissolvable film. This would include the active ingredient as well as any of the **inactive ingredients** (e.g., excipients or additives). Examples of antioxidants include, e.g., ascorbic acid (vitamin C), vitamin A, α-tocopherol (vitamin E), beta-carotene, glutathione, ubiquinol (**coenzyme Q**), and selenium."
7. (Original) The formulation of claim 6, wherein the non-enzymatic absorption enhancer is a bile acid or salt thereof.	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) **From claim 9**. "The formulation of claim 5, wherein the detergent is selected from the group consisting of a **bile acid or a salt** thereof, and an aliphatic sulphate ester." From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme (cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability."
8. (Currently Amended) The formulation of claim 7, wherein the bile acid is	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020)

selected from the group consisting of cholic acid, deoxycholic acid, glycocholic acid, chenodeoxycholic acid, taurocholic acid, glycodeoxycholic acid, and taurodeoxycholic acid, or mixtures thereof.	**From claim 9**. "The formulation of claim 5, wherein the detergent is selected from the group consisting of a **bile acid or a salt** thereof, and an aliphatic sulphate ester." From [**0044**] "Anionic detergents typically have negatively-charged sulfate or sulfonate groups as the hydrophilic head; whereas cationic detergents contain a positively-charged ammonium group. **Bile acids, such as cholic acid, deoxycholic acid, glycocholic acid, chenodeoxycholic acid, taurocholic acid, glycodeoxycholic acid, taurodeoxycholic acid, or a salts thereof**, and aliphatic sulphate esters (e.g., sodium dodecyl sulphate or sodium lauryl sulfate) are examples of anionic detergents, and quaternary ammonium salts of acetates, chlorides, or bromides are examples of cationic detergents." From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme (cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability."
9. (Currently Amended) The formulation of claim 6, wherein the non-enzymatic absorption enhancer is selected from the group consisting of bile acid, polyoxyethylene ethers, polyoxyethylene alcohols; alkali metal alkyl	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) **From claim 9**. "The formulation of claim 5, wherein the detergent is selected from the group consisting of a **bile acid or a salt** thereof, and an aliphatic sulphate ester." From [**0045**] "Non-ionie detergents have a neutral, polar head group. Non-ionic detergents are typically based on **polyoxyethylene** or a

sulfates, lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, oleic acid, linoleic acid, linolenic acid, monoolein, monooleates, monolaurates, borage oil, evening of primrose oil, chamomile extract, cucumber extract, menthol, trihydroxy oxo cholanylglycine, lysine, polylysine, triolein, polidocanol alkyl ethers, and mixtures thereof.	glycoside…" From [**0051**] "The present formulation also includes an emulsifying agent such as triethanolamine stearate, quaternary ammonium compounds, acacia, gelatin, **lecithin**, bentonite, veegum, and the like, in amounts ranging from about 0.01 to about 5 wt %, and preferably about 0.01 to about 0.7 wt % of the formulation." **From Claim 10** "The formulation of claim 1, comprising 0.01 to about 12 wt % of a saliva stimulating agent selected from citric acid, **lactic acid**, malic acid, succinic acid, ascorbic acid, adipic acid, fumaric acid, tartaric acid, and mixtures thereof." From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme (cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability."
10. (Original) The formulation of claim 1, wherein the pharmaceutical agent is selected from the group consisting of an anti-inflammatory agent, an opioid analgesic, a psychedelic drug, a cannabinoid, and a	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or

terpene.	gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
11. (Original) The formulation of claim 1, wherein the pharmaceutical component comprises two or more pharmaceutical agents.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for**

	active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
12. (Original) The formulation of claim 11, wherein the pharmaceutical component comprises a multi-modal combination of pharmaceutical agents selected from the group consisting of an anti-inflammatory agent, an opioid analgesic, a psychedelic drug, a	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass**

cannabinoid, and a terpene.	**effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0012**] "The oral dissolvable film described herein can include a single film matrix. Alternatively, **the oral dissolvable film can include multiple (e.g., 2, 3, 4, etc.) film matrices.** When the oral dissolvable film includes multiple film matrices, any one or more of the film matrices can independently be composed of the same substances present in the other film matrices. Alternatively, any one of the matrices can independently be composed of different substances present in the other film matrices (e.g., non-uniform distribution of substances in the thickness direction among the multiple film matrices)." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
13. (Original) The formulation of claim 11, wherein the multi-	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021)

modal combination results in a reduction in the dosage of at least one of the pharmaceutical agents in comparison to the dosage of the at least one pharmaceutical agent when used alone.	From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0012**] "The oral dissolvable film described herein can include a single film matrix. Alternatively, **the oral dissolvable film can include multiple (e.g., 2, 3, 4, etc.) film matrices.** When the oral dissolvable film includes multiple film matrices, any one or more of the film matrices can independently be composed of the same substances present in the other film matrices. Alternatively, any one of the matrices can independently be composed of different substances present in the other film matrices (e.g., non-uniform distribution of substances in the thickness direction among the multiple film matrices)." From [**0007**] "The present invention also provides for a method of orally administering to a subject an oral dissolvable film described herein, wherein the **oral dissolvable film includes a low dose or microdose of the psychedelic compound**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f)

	0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
14. (Original) The formulation of claim 12, comprising psilocybin.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0012**] "The oral dissolvable film described herein can include a single film matrix. Alternatively, **the oral dissolvable film can include multiple (e.g., 2, 3, 4, etc.) film matrices.** When the oral dissolvable film includes multiple film matrices, any one or more of the film matrices can independently be composed of the same substances present in the other film matrices. Alternatively, any one of the matrices can independently be composed of different substances present in the other film matrices (e.g., non-uniform distribution of substances in the thickness direction among the multiple film matrices)." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of

	benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
15. (Currently Amended) The formulation of claim 12, comprising a cannabinoid selected from the group consisting of cannabidiol, tetrahydrocannabinol (CBD, THC), and a mixture thereof.	3. U.S. Pat. App. Pub. No. US/2019/0192498 "Psilocybin composition" (Published June 27, 2019) From **Claim 1.** "**A composition comprising: 0.1 mg to 10 mg of psilocybin or psilocin**; an extract of Hericium erinaceus comprising 50 mg to 200 mg of erinacines or hericenones; and 199 mg of one or more medicinal mushroom species of Inonotus mycelia, fruitbodies, mycelial extracts, fruitbody extracts, or combinations thereof." From **Claim 5. "The composition of claim** 1, **wherein the composition further comprises one or more extracts of**: Bacopa monnieri, Centella asiatica, Gingko biloba, Zingiber officinale, Ocimum sanctum, Polygonum cuspid atum, Origanum vulgare, Origanum onites, Rosmarinus species, Curcuma longa, Camellia sinensis, Lavandula species, Scutellaria lateriflora, Avena sativa, Avena byzantine, Salvia divinorum, Banisteriopsis caapi, Psychotria species, Tabemanthe iboga, Voacanga africana, Tabemaemontana undulate, Ipomoea tricolor, Argyreia ervosa, **Cannabis sativa, Cannabis indica,** Cannabis ruderalis, or combinations thereof." From [**0019**] "Additional pharmaceutical excipients useful for the compositions as described herein include, for example, the following:.. **plasticizers** (e.g., castor oil, diacetylated monoglycerides, diethyl phthalate, glycerol, mono- and di-acetylated monoglycerides, propylene glycol, triacetin, triethyl citrate); **polymers** (e.g., cellulose acetate, alkyl celluloses, hydroxyalkyl, acrylic polymers and copolymers);… **alginate**, silicon dioxide, colloidal silicon dioxide, sodium alginate,… This list is

	not meant to be exclusive, but instead merely representative of the classes of excipients and the particular excipients that may be used in **oral dosage forms** as described herein."
16. (Currently Amended) The formulation of claim 12, comprising an opioid analgesic.	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) From [**0015**] "The present formulation comprises a water-insoluble or poorly insoluble pharmaceutical agent… **Examples of water-insoluble pharmaceutical agents include**, but are not limited to:… **n. opioid analgesics** such as alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenoorphine, butorphanol, clonitazene, codeine…" From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability." 1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0012**] "The oral dissolvable film described herein can include a single film matrix. Alternatively, **the oral dissolvable film can include multiple (e.g., 2, 3, 4, etc.) film matrices.** When the oral dissolvable film includes multiple film matrices, any one or more of the film matrices can independently be composed of the same substances present in the other film matrices. Alternatively, any one of the matrices can independently be composed of different substances present in the other film matrices (e.g., non-uniform distribution of substances in the thickness direction among the multiple film matrices)."

	From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of **psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
17. (Currently Amended) The formulation of claim 1, wherein the pharmaceutical agent is psilocybin, and the absorption enhancer is lingual lipase and sodium deoxycholate.	2. U.S. Pat. App. Pub. No. US/ 2020/0375938 "Water Soluble Formulation" (Published December 3, 2020) From [**0009**] "**A formulation that provides enhanced oral bioavailability** of poorly water-soluble pharmaceutical agents is herein provided. The formulation comprises a pharmaceutical agent which is poorly water-soluble, a detergent, **a lipase**, a **plasticizing agent** and an emulsifying agent in an aqueous solvent." From [**0048**] "Examples of enzymes that may he used in conjunction with the detergent to provide a biological detergent include, but are not limited to, **lipases such as pancreatic lipase (PL), pancreatic lipase-related protein 1 or 2 (PLRP1/PLRP2), hepatic lipase, endothelial lipase, lipoprotein lipase, lysosomal lipase, gastric lipase and lingual lipase.** Other examples include termamyl (amylase), lipolase (lipase), celluzyme

	(cellulase), mannanase and pectinase. The enzymes may be naturally occurring enzymes or recombinant enzymes. Individual enzymes or combinations of enzymes may be used." From [**0003**] "However, the **oral bioavailability** of such phytocannabinoids is limited. For example, the oral bioavailability of cannabinoids was found to be about 6% or less. The limited bioavailability of phytocannabinoids is believed to be due to the fact that cannabinoids are naturally hydrophobic, fat-soluble compounds which limits their **absorption**, thereby substantially decreasing their bioavailability." 1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From [**0012**] "The oral dissolvable film described herein can include a single film matrix. Alternatively, **the oral dissolvable film can include multiple (e.g., 2, 3, 4, etc.) film matrices.** When the oral dissolvable film includes multiple film matrices, any one or more of the film matrices can independently be composed of the same substances present in the other film matrices. Alternatively, any one of the matrices can independently be composed of different substances present in the other film matrices (e.g., non-uniform distribution of substances in the thickness direction among the multiple film matrices)." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose,

	polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, **and combinations thereof**."
18. (Currently Amended) The formulation of claim 1, wherein the hydrophilic polymer base comprises a hydrophilic elastomeric polymer selected from the group consisting of pullulan, hydroxypropyl methylcellulose, alginate, and combinations thereof, and a plasticizer comprising glycerin.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and

	combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
19. (Currently Amended) The formulation of claim 1, wherein the pharmaceutical agent is psilocybin, the absorption enhancer comprises lingual lipase and sodium deoxycholate, and wherein the hydrophilic polymer base comprises a film-forming agent selected from the group consisting of pullulan, hydroxypropyl methylcellulose, alginate, and combinations thereof.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt. % sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof."

	From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."
20. (Currently Amended) The formulation of claim 1, wherein the hydrophilic polymer base comprises pullulan and optionally additional polysaccharide-based polymers in an amount of about 50-80% by wt of the polymer base and glycerin in an amount of about 10-40% by wt of the polymer base; and the pharmaceutical component comprises a lipase absorption enhancer in an amount of about 0.1-0.5% by wt of the pharmaceutical component, bile acid in an amount of about 0.1-5% by wt of the pharmaceutical component, and psilocybin in an amount of about 0.1-1% by wt.	1. U.S. Pat. App. Pub. No. US/2021/0015738 "ORAL DISSOLVABLE FILM CONTAINING PSYCHEDELIC COMPOUND" (Published January 21, 2021) From **[0011]** "As such, **the oral dissolvable film is typically prepared using hydrophilic polymers** (e.g., film forming polymers) that dissolve on the tongue or buccal cavity, delivering the active ingredient to the systemic circulation via dissolution when contact with liquid is made. Oral film drug delivery accordingly uses a dissolving film to administer active ingredients via absorption in the mouth (buccally, sublingually, or gingivally) and/or via the small intestines (enterically). **Especially for active ingredients which are metabolized extensively by the first-pass effect, oral films described herein provide an opportunity for a faster-acting and better absorption profile**." From **[0187]** "In specific embodiments, **the oral dissolvable film includes: (a) plasticizer** selected from the group consisting of glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, and tributyl citrate, (b) solvent selected from the group consisting of water, ethanol, and combinations thereof, (c) sweetener, (d) flavoring agent, **(e) binder selected from the group consisting of** pectin, pullulan, starch, pregelatinized starch, gelatin, **polyvinylpyrrolidone**, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols, (f) coloring agent, (g) preservative selected from the group consisting of benzoate salt, sorbate salt, natamycin, and combinations thereof, and (h) **psychedelic compound selected from the group consisting of psilocybin, psilocin**, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From [**0118**] "In specific embodiments, the **psychedelic** compound is present in **0.01-1 wt. % of the oral dissolvable film**." From [**0147**] "In specific embodiments, the oral dissolvable film contains 8±3 wt. % residual solvent." From **[0188]** "In specific embodiments, the **oral dissolvable film includes**: **(a) 10±5 wt. % plasticizer**, (b) 8±5 wt. % solvent, (c) 10±5 wt.

	% sweetener, (d) 8±5 wt. % flavoring agent, **(e) 25±10 wt. % binder**, (f) 0.02±0.01 wt. % coloring agent, (g) 0.02±0.01 wt. % preservative, and (h) 17±16.5 wt. % psychedelic compound selected from the group consisting of psilocybin, psilocin, baeocystin, mescaline, LSD, ketamine, salvinorin A, ibotenic acid, muscimol, DMT, MDMA, MDEA, MDA, and combinations thereof." From **[0019]** "**Suitable plasticizers include, e.g., glycerin**, water, polyethylene glycol, honey, propylene glycol, monoacetin, triacetin, triethyl citrate, sorbitol, 1,3-butanediol, D-glucono-1,5-lactone, diethylene glycol, castor oil, and combinations thereof."

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
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Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Sisi Li
PATENT CENTER #	67676828	FILING DATE	11/10/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 6

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Concise-description-generated.pdf		2	Concise Description of Relevance	26 KB
third-party-preissuance-submission.pdf		2	Third-Party Submission Under 37 CFR 1.290	44 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	13 KB
Claims_Chart.pdf		24	-	315 KB
Claims_Chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	251 KB
Claims_Chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	251 KB
Claims_Chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	251 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
Concise-description-generated.pdf	3F6B616E34D5667181F6D05109590D615E79875C2FBBD07B712D0A44AEF4A64E5865912390D2091ACA27EE5513C345E54762116B1EC1C01F9197F9D8276E2C84
third-party-preissuance-submission.pdf	734975E53D7F9A5B06FE0A505AF494A3DFA3294672448F5996A34BDBA283A673774C2EDE2859EF7EDAB0089D6D19D11BEDDB0B4B03148AEAFDF47FB58A48358A
Third-party-notification-request.pdf	442BC86981FA773B031F04F179150BEAF4014354B040A67D0D9BC3FC1D22A6BA9F4DC4B5BB333B72D6AC254F4C4DF9657A31D36177F416F52F223F133B0A0EF2
Claims_Chart.pdf	531A5160ED291B58A681513A82D247717C2898B2B5E559123456AB9B88A57E7E391FC0429067B4FD1F4437785A39E901CB8EA4030A72668880EDC2E6E8359969
Claims_Chart-3P.RELEVANCE.pdf	A77F36CBA2DF72D957A7AFF69EF2EDDA85F7E3C753A5BFCAC1F5B4D2D7C445AEB82A61CF5E9B89C456FB904B939B155C733BF0EE0E77755207DB902857F64961
Claims_Chart-3P.RELEVANCE.pdf	2C0FB7BC5C8F5FC84C54BF285DDC2DF6F5925EE479B1AB5DA1E9501ACA20C4F6454C0ACE37A33B0A4E142A4818967837C31665CA90DF901F09FF029CF0133338
Claims_Chart-3P.RELEVANCE.pdf	E177806EA657A9E2ECD7BF50295C60D4E49366B8CF3E6A6B4524459E86D03FB8BD620446D2E99335E7C00DFC613E6B2E9B7F6B37EED57AEB2D02AE9D88216F99

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