Antidepressant & Psychedelic Drug Interaction Chart

This chart is not intended to be used to make medical decisions and is for informational purposes only. It was constructed using data whenever possible, although extrapolation from known information was also used to inform risk. Any decision to start, stop, or taper medication and/or use psychedelic drugs should be made in conjunction with your healthcare provider(s). It is recommended to not perform any illicit activity.

Antidepressant	**Phenethylamines** -MDMA, mescaline	**Tryptamines** -Psilocybin, LSD	**MAOI-containing** -Ayahuasca, Syrian Rue	**Ketamine**	**Ibogaine**
SSRIs · Paroxetine (Paxil) · Sertraline (Zoloft) · Citalopram (Celexa) · Escitalopram (Lexapro) · Fluoxetine (Prozac) · Fluvoxamine (Luvox) **SPARI** · Vibryyd (Vilazodone) · Trintellix (Vortioxetine) **SNRI** ·Venlafaxine (Effexor) ·Duloxetine (Cymbalta) ·Desvenlafaxine (Pristiq) ·Levomilnacipran (Fetzima)	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to loss of psychedelic effect MDMA is unable to cause release of serotonin when the serotonin reuptake pump is blocked. This leads to drastically reduced effects [1-7]	Consider taper & discontinuation at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to potential loss of psychedelic effect Chronic antidepressant use may result in down-regulation of 5HT2A receptors and blunted psychedelic experiences [8, 9]. This does not seem to affect psilocybin for some	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to potential risk of serotonin syndrome Life threatening toxicities can occur with these combinations and is strictly contraindicated [10, 11]	Has been studied and found effective both with and without concurrent use of antidepressants Recommended to be used in conjunction with oral antidepressants by esketamine manufacturer	Taper & discontinue at least 2 weeks prior (all except fluoxetine) or 6 weeks prior (fluoxetine only) due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity Some antidepressants are liver (CYP2D6) inhibitors and have been shown to double ibogaine blood concentrations [12]

DNRI · Bupropion (Wellbutrin)	Increased effects of MDMA with higher blood concentrations for longer [13]. May increase risk of seizures in combination. Caution in combination. Consider taper & discontinuation of bupropion. Alternatively, a 25% reduced dose of MDMA if bupropion is continued.	Loss of effect not predicted to occur, consider taper & discontinuation depending on goals of psychedelic use	Taper & discontinue at least 2 weeks prior due to potential of adverse effects, however serotonin syndrome unlikely to occur [14]		Taper & discontinue at least 2 weeks prior to use. May increase risk of seizures in combination. CYP2D6 inhibitor with potential to increase ibogaine blood concentrations
· Mirtazapine (Remeron)	Taper & discontinue at least 2 weeks prior due to loss of psychedelic effect Mirtazapine does not block the serotonin reuptake pump like SSRI, SPARI, or SNRI antidepressants. It blocks the 5HT2A receptor, thus is predicted to cause a blunting or loss of psychedelic effects. It has not been associated with serotonin syndrome with MAOIs [14]				Taper & discontinue at least 2 week prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity

SSRI = selective serotonin reuptake inhibitor SPARI = serotonin partial agonist and reuptake inhibitor SNRI = serotonin norepinephrine reuptake inhibitor DNRI = dopamine norepinephrine reuptake inhibitor MAOI = monoamine oxidase inhibitor SERT = serotonin reuptake pump 5HT2A = serotonin 2A receptor

Antidepressant	**Phenethylamines** -MDMA, mescaline	**Tryptamines** -Psilocybin, LSD	**MAOI-containing** -Ayahuasca, Syrian Rue	**Ketamine**	**Ibogaine**

Tricyclic Antidepressant (TCA) · Amitriptyline (Elavil) · Nortriptyline (Pamelor) · Clomipramine (Anafranil) · Imipramine (Tofranil) · Desipramine (Norpramin) · Chlorpheniramine	Taper & discontinue at least 2 weeks prior due to loss of psychedelic effect MDMA is unable to cause release of serotonin when the serotonin reuptake pump is blocked. This leads to drastically reduced effects	Consider taper & discontinuation at least 2 weeks prior due to potential intensified effects Chronic TCA use was reported to increase the subjective effects of LSD [15]	Taper & discontinue at least 2 weeks prior due to potential risk of serotonin syndrome. Risk is highest with clomipramine, imipramine, and chlorpheniramine [14] Life threatening toxicities can occur with these combinations and is strictly contraindicated	Has been studied and found effective both with and without concurrent use of antidepressants Recommended to be used in conjunction with oral antidepressants by esketamine manufacturer	Taper & discontinue at least 2 weeks prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity Some antidepressants are liver (CYP2D6) inhibitors and have been shown to double ibogaine blood concentrations
· Trazodone (Desyrel)	Taper & discontinue at least 5 days prior due to loss of psychedelic effect Trazodone blocks 5HT2A receptors at lower doses (25-150mg) and starts blocking the serotonin reuptake pump (SERT) at >150mg [14]. It has an active metabolite that also blocks 5HT2A receptors as well as modulating many other 5HT receptors				Taper & discontinue at least 1 week prior due to risk of additive QTc interval prolongation, arrhythmias, or cardiotoxicity
· Buspirone (Buspar)	Taper & discontinue at least 5 days prior due to loss of psychedelic effect Buspirone is a non-psychedelic partial agonist at serotonin receptors, thus may display blunting of psychedelic effects due to competitive inhibition when used in combination with psychedelics [16]. It does not inhibit the reuptake of nor release neurotransmitters, thus risk of serotonin syndrome with MAOIs is low				Taper & discontinue at least 5 days prior due to potential risk of toxicity
MAO-A Inhibitors* · Phenelzine (Nardil) · Isocarboxazid (Parnate) · Tranylcypromine (Marplan) · Moclobemide *chronic use	Taper & discontinue at least 2 weeks prior due to potential risk of serotonin syndrome or hypertensive crisis [17]	Consider taper & discontinuation at least 2 weeks prior due to potential loss of psychedelic effect [15] Contraindicated with tryptamine 5-MeO-DMT [18, 19]	Taper & discontinue at least 2 weeks prior Additive use of MAOIs may cause intensified experiences or cardiovascular collapse (fainting or dangerously low blood pressure)		Taper & discontinue at least 10 days prior due to potential risk of toxicity [20]

MAO-B inhibitors · Selegeline (Emsam)	Intensified effects, risk of serotonin syndrome at doses ≥9mg/day Taper & discontinue at least 2 weeks prior, especially if dose ≥9mg/day	Intensified effects possible, risk of serotonin syndrome at doses ≥9mg/day with 5-MeO DMT; psilocybin or LSD likely have low risks of physical toxicity in combination			

SSRI = selective serotonin reuptake inhibitor SPARI = serotonin partial agonist and reuptake inhibitor SNRI = serotonin norepinephrine reuptake inhibitor DNRI = dopamine norepinephrine reuptake inhibitor MAOI = monoamine oxidase inhibitor SERT = serotonin reuptake pump 5HT2A = serotonin 2A receptor

References:

1. Farre, M., et al., *Pharmacological interaction between 3,4-methylenedioxymethamphetamine (ecstasy) and paroxetine: pharmacological effects and pharmacokinetics.* J Pharmacol Exp Ther, 2007. **323**(3): p. 954-62.

2. Hysek, C.M., et al., *Duloxetine inhibits effects of MDMA ("ecstasy") in vitro and in humans in a randomized placebo-controlled laboratory study.* PLoS One, 2012. **7**(5): p. e36476.

3. Liechti, M.E. and F.X. Vollenweider, *The serotonin uptake inhibitor citalopram reduces acute cardiovascular and vegetative effects of 3,4-methylenedioxymethamphetamine ('Ecstasy') in healthy volunteers.* J Psychopharmacol, 2000. **14**(3): p. 269-74.

4. Piper, B.J., et al., *Dissociation of the neurochemical and behavioral toxicology of MDMA ('Ecstasy') by citalopram.* Neuropsychopharmacology, 2008. **33**(5): p. 1192-205. 5. Stein, D.J. and J. Rink, *Effects of "Ecstasy" blocked by serotonin reuptake inhibitors.* J Clin Psychiatry, 1999. **60**(7): p. 485.

6. Tancer, M. and C.E. Johanson, *The effects of fluoxetine on the subjective and physiological effects of 3,4-methylenedioxymethamphetamine (MDMA) in humans.* Psychopharmacology (Berl), 2007. **189**(4): p. 565-73.

7. Gudelsky, G.A. and J.F. Nash, *Carrier-mediated release of serotonin by 3,4-methylenedioxymethamphetamine: implications for serotonin-dopamine interactions.* J Neurochem, 1996. **66**(1): p. 243-9.

8. Bonson, K.R., J.W. Buckholtz, and D.L. Murphy, *Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans.* Neuropsychopharmacology, 1996. **14**(6): p. 425-36.

9. Carhart-Harris, R.L. and D.J. Nutt, *Serotonin and brain function: a tale of two receptors.* Journal of Psychopharmacology (Oxford, England), 2017. **31**(9): p. 1091-1120. 10. Callaway, J.C. and C.S. Grob, *Ayahuasca preparations and serotonin reuptake inhibitors: a potential combination for severe adverse interactions.* J Psychoactive Drugs, 1998. **30**(4): p. 367-9.

11. Malcolm, B.J. and K.C. Lee, *Ayahuasca: An ancient sacrament for treatment of contemporary psychiatric illness?* Ment Health Clin, 2017. **7**(1): p. 39-45. 12. Glue, P., et al., *Influence of CYP2D6 activity on the pharmacokinetics and pharmacodynamics of a single 20 mg dose of ibogaine in healthy volunteers.* J Clin Pharmacol, 2015. **55**(6): p. 680-7.

13. Schmid, Y., et al., *Interactions between bupropion and 3,4-methylenedioxymethamphetamine in healthy subjects.* J Pharmacol Exp Ther, 2015. **353**(1): p. 102-11. 14. Gilman, K., *Monoamine oxidase inhibitors: A review concerning dietary tyramine and drug interactions.* PsychoTropical Commentaries, 2017. **1**(1): p. 105. 15. Bonson, K.R. and D.L. Murphy, *Alterations in responses to LSD in humans associated with chronic administration of tricyclic antidepressants, monoamine oxidase inhibitors or lithium.* Behav Brain Res, 1996. **73**(1-2): p. 229-33.

16. Pokorny, T., et al., *Modulatory effect of the 5-HT1A agonist buspirone and the mixed non-hallucinogenic 5-HT1A/2A agonist ergotamine on psilocybin-induced psychedelic experience.* Eur Neuropsychopharmacol, 2016. **26**(4): p. 756-66.
17. Pilgrim, J.L., et al., *Serotonin toxicity involving MDMA (ecstasy) and moclobemide.* Forensic Sci Int, 2012. **215**(1-3): p. 184-8.
18. Callaway, J.C., et al., *A demand for clarity regarding a case report on the ingestion of 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) in an Ayahuasca preparation.* J Anal Toxicol, 2006. **30**(6): p. 406-7; author reply 407.
19. ICEERS, *Risks associated with combining Bufo Alvarius with ayahuasca.* 2017.
20. Global Ibogaine Therapy Alliance. *Clinical Guidelines for Ibogaine-Assisted Detoxification*. 2015 [cited 2017 June 27th]; Available from: https://www.ibogainealliance.org/guidelines/.