Psychedelics and mindfulness: A systematic review and meta-analysis

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ABSTRACT

Background and aims: The benefits of classic serotonergic psychedelics (e.g. psilocybin, LSD, DMT, ayahuasca) are becoming more widely known with the resurgence in research in the past decade. Furthermore, the benefits of mindfulness are well documented. However, no systematic reviews have examined linkage of mindfulness and psychedelics use. The aim of this systematic review is to explore the link between psychedelics and characteristics of mindfulness.

Methods: We conducted a systematic search across multiple databases, inclusive of grey literature and backwards/forward-citation tracking, on the 18 January 2021. The search strategy included terms relating to mindfulness and psychedelics, with no restriction on clinical or non-clinical conditions. Study quality was assessed. An exploratory random-effects meta-analysis was conducted on pre-post mindfulness data relative to psychedelic ingestion.

Results: Of 1805 studies screened, 13 were included in the systematic review. There was substantial variability in participant characteristics, psychedelic administration method and measurement of mindfulness. The ingestion of psychedelics is associated with an increase in mindfulness, specifically relating to domains of acceptance, which encompasses non-judgement of inner experience and non-reactivity. The meta-analysis of a subset of studies (N = 6) showed small effects overall relative to ayahuasca ingestion, increasing mindfulness facets of non-judgement of inner experience and non-reactivity, as well as acting with awareness.

Conclusions: Further methodologically robust research is needed to elucidate the relationship between psychedelics and mindfulness. However, mindfulness and specific facets relating to acceptance have been shown to increase following ingestion of psychedelics in a number of studies.

KEYWORDS

psilocybin, ayahuasca, mindfulness, systematic review, meta-analysis

INTRODUCTION

The term psychedelic was coined by Humphrey Osmond in 1957 in order to describe their mind-manifesting capabilities, using a combination of the Greek words psyche (mind) and delos (manifest) (Osmond, 1957). Classic psychedelic substances include N,N-Dimethyltryptamine (DMT), found in the Amazonian brew ayahuasca; psilocybin, found in many species of mushrooms; mescaline, found in the peyote cactus; and lysergic acid diethylamide (LSD), which is synthesized. These psychedelics produce a variety of subjective experiences: changes in perception, volition, cognition, thinking and mood, along with visual and auditory hallucinations, and dissociative phenomena are all possible effects of these psychedelics (Isbell, 1959; Riba et al., 2001; Wolbach, Miner, & Isbell, 1962).

Psychedelics are in the midst of a revival of research and understanding (Carhart-Harris & Goodwin, 2017). Psychedelics’ beneficial role in healthcare and well-being is historically...
well established (Nichols, 2016), and their positive effects on clinical populations are increasingly highlighted (Bogenschutz et al., 2015; Carhart-Harris et al., 2018; Griffiths et al., 2016; Sanches et al., 2016; Thomas et al., 2013). Further, the importance of set (e.g. mindset, beliefs, attitudes, expectations, motivation) and setting (e.g. physical, social, cultural context) have been identified as essential components of therapeutic use of psychedelics. They can minimise adverse reactions and support beneficial therapy (Eisner, 1997). Currently, there are more controlled trials than ever before (Doblin, Christiansen, Jerome, & Burge, 2019). The potentially beneficial role of psychedelics is now being more broadly considered in response to current research highlighting positive effects on, for example, cancer-related anxiety and depression (Griffiths et al., 2016), addiction (Bogenschutz et al., 2015; Thomas et al., 2013), and major depressive disorder (Carhart-Harris et al., 2018; Sanches et al., 2016). These studies have laid the groundwork for psychedelics to become a serious option in the treatment of a variety of clinical populations and for increased well-being in healthy individuals (Nicholas et al., 2018; Schmid & Liechti, 2018).

Existing research has explored whether psychedelics enhance well-being in healthy populations and examined reported experiences of phenomena such as mindfulness (Elsey, 2017). Mindfulness is defined as “awareness that arises through paying attention, on purpose, in the present moment, non-judgmentally” (Kabat-Zinn, 1994, p. 4) and has its roots in contempative traditions, specifically Buddhism (Shapiro, Carlson, Astin, & Freedman, 2006). Mindfulness is an umbrella term that includes many practices and processes, relating to attention, awareness, acceptance, attitude and memory (Shapiro et al., 2006; Van Dam et al., 2018). Measuring mindfulness constructs can be done using a variety of psychometric outcome measures (Park, Reilly-Spong, & Gross, 2013) such as the Five Facets of Mindfulness Questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) or the Philadelphia Mindfulness Scale (PHILMS; Cardaciotto, Herbert, Forman, Moitra, & Farrow, 2008). For example, the FFMQ measures observation (seeing, feeling and perception of internal or external experiences), description (labelling and expression of experiences), acting with awareness (attention to present moment experiences), non-judgmental inner experience (acceptance of self and empathy to others) and non-reactivity (emotional resilience and detachment from negativity). There are a number of psychological interventions integrating mindfulness principles for therapeutic use including Mindfulness-Based Stress Reduction (MBSR; Kabat-Zinn, 1990), Dialectical Behavioural Therapy (DBT; Linehan, 1993), and Acceptance and Commitment Therapy (ACT; Hayes, Luoma, Bond, Masuda, & Lillis, 2006). Further, there have been studies showing the wide-ranging benefits of mindfulness for the treatment of conditions ranging from chronic pain and substance abuse to general well-being (Bowen et al., 2009; Kabat-Zinn, Lipworth, & Burney, 1985; Kingston, Chadwick, Meron, & Skinner, 2007; Ramirez-Barrantes et al., 2019).

A review by Jungaberle, et al. (2018) found that psychedelics may be able to sustain and enhance aspects such as mood, wellbeing, openness and flexibility, as well as mindfulness-related capabilities. While a state of mindfulness can be cultivated through dedicated practice or psychological therapy, this may be further facilitated through use of psychedelic substances. A more recent review and meta-analysis by Goldberg et al. (2020) also supports the hypothesis that psychedelics increase mindfulness, however, there are currently no systematic reviews examining the link between psychedelic use and its effect on facets or characteristics of mindfulness. Previous narrative reviews have emphasised the importance of integration of mindfulness interventions and psychedelics (Payne, Chambers, & Liknaitzky, 2021; Walsh & Thiessen, 2018). More recently synergistic use of mindfulness training and psychedelic-assisted therapy have been suggested as potential effective avenues management of mental health problems, such as anxiety and depression (Felsch & Kuypers, 2022; Heuschkel & Kuypers, 2020).

Therefore, the aims of this systematic review were to investigate the relationship between psychedelic use and an increase in mindfulness in clinical and non-clinical populations, and to explore the effects of psychedelic use on facets or characteristics of mindfulness. Further, the aim was to conduct a meta-analysis to investigate if there might be any consistent effect relative to use of psychedelics and different facets of mindfulness.

METHODS

The systematic review protocol was registered with PROSPERO and published online: https://www.crd.york.ac.uk/prospero/display_record.php?ID = CRD42019160973. This review was conducted according to PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & Grp, 2009).

Eligibility criteria

Eligibility criteria for inclusion in the systematic review were primary and secondary studies (including grey literature) written in the English language, that measured mindfulness in the context of psychedelic substance use for people above the age of 18. All study designs, except systematic reviews, were eligible. There were no restrictions relating to participant population, with studies recruiting healthy and clinical populations being eligible. Exclusion criteria were systematic reviews, editorials and conference proceedings.

Information sources and search strategies

A systematic search was initially conducted including studies available up to 10 December 2019. A second search was completed on 18 January 2021 to update search results. This systematic review used primary databases (MEDLINE and Embase via OVID), specialised databases (PsycINFO and AMED via EBSCO). Forward citation tracking from key relevant articles (Scopus), backward citation tracking using references of included articles, the MAPS (Multidisciplinary
Association of Psychedelic Studies) Bibliography, websites of known research organisations and retreats who provide guided use of psychedelics with a research link (e.g. Temple of the Way of the Light), and contact with study authors.

Search terms included medical subject headings (MeSH) and keywords. The first search terms were descriptive of the intervention, relating to psychedelic substances terms ('hallucinogens' OR 'psychedelic' OR 'psychoactive' OR 'psychotomimetic' OR 'psychotogenic' OR 'psyilocybin' OR 'mescaline' OR 'peyote' OR 'magic mushroom' OR 'LSD' OR 'lysergic acid diethylamide' OR 'DMT' OR 'N,N-Dimethyltryptamine' OR 'ayahuasca'). The AND operator was used for the second set of terms, which were descriptive of outcome, relating to mindfulness ('mindfulness' OR 'meditation' OR 'attention' OR 'consciousness' OR 'vipassana').

**Study screening**

Initial searches in databases were performed and duplicate results were removed. Following this, two reviewers independently screened titles and abstracts based on eligibility and exclusion criteria. Any disagreements were resolved through discussion between the two reviewers. Following this, full text articles were then screened and assessed for eligibility independently by two reviewers and any disagreements on inclusion resolved through discussion between the two reviewers.

**Data collection**

The data extracted from the included articles were study design, clinical condition (if any), intervention(s) in study, sub-groups/control group, population size, demographics, aims of study, mindfulness measure used, and results. Quantitative data extracted included means of pre and post intervention groups, standard deviations of pre and post intervention groups, population size, effect size, and p-values.

**Quality appraisal**

Quality of individual studies was assessed using the National Heart, Lung, and Blood Institute Study Quality Assessment Tools (National Heart Lung and Blood Institute, 2018). Study quality was assessed by two reviewers independently and any disagreements were resolved through discussion. If a resolution could not be reached, the study was sent to a third reviewer for adjudication.

**Statistical analysis**

Extracted data and quality assessment ratings underwent data synthesis and descriptive comparison. R Software (RStudio Team, 2020) using the meta package, was utilised to perform an exploratory random-effect meta-analysis (Anello & Fleiss, 1995). Studies included in the meta-analysis were of a pre-post design, containing a psychedelic intervention and consisting of complete data on all mindfulness construct/subconstructs measured (e.g. FFMQ). Standardised mean difference, 95% confidence intervals, and percent weight were calculated for studies eligible for meta-analysis. For studies without numerical data provided, authors were contacted on two occasions. We were unable to obtain numerical data from these attempts so mean and standard error data were extracted from graphs (Rohatgi, 2021), following which standard deviation was estimated (Higgins & Thomas, 2019). This was done by plotting the available graphs (without detailed x or y axes) onto graphs with more detailed axes in order to estimate the numerical data. Where studies had more than one intervention group, standard deviations and means were pooled (Higgins & Thomas, 2019).

Heterogeneity between studies was assessed prior to choosing a fixed or random effects model using Q (or χ²) statistic, I² and prediction intervals. Q represents the presence of heterogeneity while I² describes the variability in effect estimates due to heterogeneity as opposed to sampling error (Higgins & Thomas, 2019). A significant Q value (P < 0.0035) represented the presence of heterogeneity in the studies while a high I² value 74.5% indicated the extent of heterogeneity. I² values between 0–25 were classified as absent, 25–50 as low, 50–75 as medium, and 75–100 as high heterogeneity (Borenstein, Hedges, Higgins, & Rothstein, 2010). Prediction intervals were also used to help with clinical interpretation of the heterogeneity through estimation of what true treatment effects can be expected in future settings (IntHout, Ioannidis, Rovers, & Goeman, 2016).

**RESULTS**

**Search results**

The searches identified a total of 1805 records from databases and other sources with a total of 13 studies meeting inclusion criteria (Dominguez-Clave et al., 2019; Madsen et al., 2020; Mian, Altman, & Earleywine, 2019; Murphy-Beiner & Soar, 2020; Polito & Stevenson, 2019; Sampedro et al., 2017; Smigielski et al., 2019; Soler et al., 2016, 2018; Thomas et al., 2013; Uthaug et al., 2018, 2019, 2020). Figure 1 shows the full screening process including reasons for exclusion of articles.

Table 1 shows the characteristics of all included studies. Substances studied were ayahuasca – 8 (Dominguez-Clave et al., 2019; Mian et al., 2019; Murphy-Beiner & Soar, 2020; Sampedro et al., 2017; Soler et al., 2016, 2018; Thomas et al., 2013; Uthaug et al., 2018), psilocybin – 2 (Madsen et al., 2020; Smigielski et al., 2019), 5-MeO-DMT – 2 (Uthaug et al., 2019, 2020), and mixed serotonergic psychedelics (LSD, Psilocybin, Mescaline, other) – 1 (Polito & Stevenson, 2019). Eleven of the included studies were pre-post intervention design with no control group (Dominguez-Clave et al., 2019; Madsen et al., 2020; Murphy-Beiner & Soar, 2020; Polito & Stevenson, 2019; Sampedro et al., 2017; Soler et al., 2016, 2018; Thomas et al., 2013; Uthaug et al., 2018, 2020, 2019). The two remaining studies were a cross-sectional survey (Mian et al., 2019) and a randomised controlled trial.
The timeframe of follow-up assessment using mindfulness outcome measures was as follows: of the 12 studies (eleven pre-post study and one randomized control study), 75% (N = 9) collected mindfulness outcome measurements immediately after or approximately 24 h after ingestion, with the remaining 25% (N = 3) of studies doing this between 2 weeks and 3 months after ingestion. Further longer-term follow-up mindfulness assessments were performed in 41.7% (N = 5) of studies, the timeframe of which ranged from 1 week to 6 months. The total number of participants included over all studies was 530 with an overall range from 10 to 152. The mean age of participants, calculated from 10 of 13 studies, as two reported ranges (Mian et al., 2019; Polito & Stevenson, 2019) and one did not report age (Uthaug et al., 2018), was 44.9 years with a standard deviation of 1.6 years. Mean percentage of males was 53.4% across twelve studies with a standard deviation of 14%. Three studies included participants with clinical conditions; depression (Mian et al., 2019), borderline personality disorder-like (Domínguez-Clavé et al., 2019), and addiction (Thomas et al., 2013), while the remaining ten studies included participants with no reported clinical condition (Madsen et al., 2020; Murphy-Beiner & Soar, 2020; Polito & Stevenson, 2019; Sampedro et al., 2017; Smigielski et al., 2019; Soler et al., 2016, 2018; Uthaug et al., 2018, 2019, 2020).

Quality appraisal
See Appendix 1 Table A1 full quality appraisal results. The overall quality of included studies was fair. All of the studies described their objectives well, used appropriate and valid outcome measures consistently, and statistical methods to analyse the results were reported clearly. The sample sizes in included studies were moderate, although sample size calculations were not made clear in the majority of studies, somewhat restricting the generalisability of findings to a wider population. A primary issue in the majority of studies was consistency of intervention delivery across participants where numbers of doses and quantities per dose varied.

Methodological weaknesses included those inherent in the study designs while others were acquired through the research process. In some cases, weaknesses in the study were due to the nature and tradition of ayahuasca ingestion, which includes for example, variations in dose, setting, and consistency in the delivery of the intervention from participant to participant (Domínguez-Clavé et al., 2019;
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Condition</th>
<th>Intervention/ Additional Intervention</th>
<th>Control/ Subgroups</th>
<th>Sample size</th>
<th>Participants</th>
<th>Aims of study</th>
<th>Mindfulness Outcome Measure</th>
<th>Mindfulness Results</th>
<th>Time-frame (Post and Follow-up)</th>
<th>Quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domínguez-Clavé et al. (2019)</td>
<td>Observational, pre/post intervention</td>
<td>BPD-like</td>
<td>Ayahuasca</td>
<td>BPD and non-BPD</td>
<td>$n = 45$  ($N = 13$)</td>
<td>Recruited through three groups planning to have ayahuasca ceremonies in Barcelona. Sex: $F = 27$, $M = 18$ Age: $m = 40$ One-third of the participants were ayahuasca-naïve.</td>
<td>To assess the effects of ayahuasca on emotion regulation. BPD status assessed by researchers.</td>
<td>FFMQ – Short Form (24)</td>
<td>Statistically significant differences pre/post with large effect sizes in the FFMQ-SF subscales: Non-judgmental inner experience ($\eta^2 = 0.28$) Non-reactivity ($\eta^2 = 0.20$) Observing ($\eta^2 = 0.63$) Acting with awareness ($\eta^2 = 0.24$)</td>
<td>Post (in a 24 h period)</td>
<td>Poor</td>
</tr>
<tr>
<td>Madsen et al. (2020)</td>
<td>Pre/post intervention</td>
<td>Non-clinical</td>
<td>Psilocybin</td>
<td>None</td>
<td>$n = 10$</td>
<td>Recruited from list of interested volunteers. Sex: $M = 6$, $F = 4$ Age: $m = 28$ (SD 3.4) All psychedelic-naïve.</td>
<td>To evaluate underlying mechanisms for long-term effects of psilocybin, and investigate the effects of psilocybin on mindfulness and personality three months following psilocybin intake.</td>
<td>MAAS</td>
<td>No results were considered significant for $P$ values $&lt; 0.05$ Mindfulness significantly increased at follow-up ($P = 0.023$)</td>
<td>Post (3 months)</td>
<td>Fair</td>
</tr>
<tr>
<td>Mian et al. (2019)</td>
<td>Cross-sectional survey</td>
<td>Depression</td>
<td>Ayahuasca (Retrospective survey)</td>
<td>None</td>
<td>$n = 152$</td>
<td>Recruited via Facebook. Sex: $M = 50.7$% Age: $r = 40–49$ Ethnicity: 86.2% white Level of education: &gt;50% completed Bachelor or graduate degree Lifetime ayahuasca use: $m = 40.2$</td>
<td>To investigate whether both mindfulness and behavioural activation might contribute to the anti-depressant effects of ayahuasca</td>
<td>NA</td>
<td>FFMQ</td>
<td>An increase in mindfulness (overall) was strongly associated ($P &lt; 0.001$) with reduced depression severity. Changes in depressive symptoms covaried with subscales from the FFMQ.</td>
<td></td>
</tr>
<tr>
<td>Murphy-Beiner and Soar (2020)</td>
<td>Observational, pre/post intervention</td>
<td>Non-clinical</td>
<td>Ayahuasca</td>
<td>None</td>
<td>$n = 48$</td>
<td>Recruited through psychedelics mailing list. Sex: $M = 22$ $F = 26$ Age: $m = 38.48$ (SD 7.21)</td>
<td>To assess changes in mindfulness, decentering, and cognitive flexibility both at baseline and 24 h following ayahuasca use</td>
<td>FFMQ – Short Form (24)</td>
<td>Significant post-ayahuasca increase in overall mindfulness ($P = 0.003$) Significant increase in scores on: Reflecting ($P &lt; 0.001$) Describe ($P = 0.03$)</td>
<td>Post (within 24 h)</td>
<td>Fair</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Design</td>
<td>Condition</td>
<td>Control/ Subgroups</td>
<td>Sample size</td>
<td>Participants</td>
<td>Aims of study</td>
<td>Intervention/ Additional Intervention</td>
<td>How many doses/ administered by whom?</td>
<td>Time-frame (Post and follow-up)</td>
<td>Mindfulness Outcome Measure</td>
<td>Mindfulness Results</td>
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<tr>
<td>Polito and Stevenson (2019)</td>
<td>Observational Pre/post intervention Uncontrolled</td>
<td>Non-clinical</td>
<td>None</td>
<td>$n = 63$ completed psychometric measures at baseline and completion</td>
<td>Recruited through Reddit and Facebook. Sex: $M = 49, F = 14$. Age: (18-25) = 13, (26-35) = 31, (36-45) = 11, (46-55) = 7, (55+) = 1. Postgraduate education = 71.4%</td>
<td>To assess the effects of micro-dosing psychedelics with the expectations of micro-dosing psychedelics. Serotonergic psychedelics (LSD-48.1%, Psilocybin-47.1%, Mescaline-2.1%, other synthetic research chemicals-2.7%). Doses were taken every 3 days and were self-administered. LSD: $m = 13.5$ μg (SD 8.5 μg) Psilocybin: $m = 0.3$ μg (SD 0.3 μg). Mescaline: $m = 2.6$ μg (SD 2.7 μg).</td>
<td>Post (6 weeks)</td>
<td>MAAS</td>
<td>No significant increase in mindfulness scores. Expectation was for an increase in mindfulness.</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>Sampedor et al. (2017)</td>
<td>Pre/post/ follow-up intervention Uncontrolled, open label</td>
<td>Non-clinical</td>
<td>None</td>
<td>$n = 16$ Follow up: $n = 14$</td>
<td>Volunteers with prior experience of ayahuasca in Barcelona area. Sex: $M = 10, F = 6$. Age: $m = 39$</td>
<td>To improve understanding of the neural mechanisms potentially involved in the rapid and sustained therapeutic effects observed in patients. Ayahuasca: One dose administered within lay context by researchers.</td>
<td>Post (24 h), Follow-up (2 months)</td>
<td>FFMQ</td>
<td>Statistically significant increases in scores on: non-judgemental inner experience ($P = 0.011$) non-reactivity ($P = 0.020$) Follow up: Statistically significant increases in scores on: Non-judgemental inner experience ($P = 0.045$)</td>
<td>Good</td>
<td></td>
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<tr>
<td>Smigielski et al. (2019)</td>
<td>Prospective matched group study Pre/post/ follow-up intervention Double blind</td>
<td>Non-clinical</td>
<td>Matched groups: Meditation and meditation with psilocybin</td>
<td>$n = 39$ (Placebo $n = 19$, psilocybin $n = 20$)</td>
<td>Recruited expert meditators through meditation communities and professional Buddhist magazines. Sex: $M = 23, F = 16$. Age: $m = 51.66$</td>
<td>To quantify the effects of meditation alone and meditation combined with psilocybin. Meditation depth, mindfulness (state and trait), mystical experience and altered states of consciousness were explored, compared and analysed for their interactions and influence on one another. Psilocybin: Standardised doses of psilocybin, according to body weight, and placebo (lactose) were administered in a double-blind setting. 315 μg kg$^{-1}$ of body weight. Administered on day 4 of 5 during meditation retreat.</td>
<td>Post (day 6, after the 5 day retreat- 24 h)</td>
<td>TMS (State mindfulness) FMI (trait mindfulness)</td>
<td>Psilocybin did not significantly increase state mindfulness ($P = 0.53$). Trait mindfulness was significantly higher post-retreat (day 6) than pre-retreat (day 0) ($P &lt; 0.001$)</td>
<td>Good</td>
<td></td>
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<tr>
<td>Soler et al. (2018)</td>
<td>Exploratory comparison study Pre/post intervention Uncontrolled</td>
<td>Non-clinical</td>
<td>Comparison groups: Ayahuasca and MBSR</td>
<td>$n = 20$ (n = 10 per group)</td>
<td>Recruited by word of mouth after initial contact in Barcelona area. Sex: $M = 3, F = 7$. Age: $m = 50$</td>
<td>To understand the therapeutic mechanisms by which Ayahuasca works by studying its impact on mindfulness-related capacities. Ayahuasca group, MBSR group</td>
<td>Post (24 h)</td>
<td>FFMQ</td>
<td>Ayahuasca led to statistically significant increases in scores on: Non-judgemental inner experience ($P &lt; 0.05$)</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Study Design</td>
<td>Condition</td>
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<td>Soler et al. (2016)</td>
<td>Pre/post intervention Uncontrolled</td>
<td>Non-clinical</td>
<td>None</td>
<td>n = 25</td>
<td>Recruited by word of mouth in Barcelona area. Sex: M = 11, F = 14 Age: m = 43.6 Years of education: m = 15 Two participants were ayahuasca-naive. Lifetime experience of ayahuasca: m = 79</td>
<td>Comparing the effects of a standard mindfulness training course with four consecutive ayahuasca sessions. To understand the psychological mechanisms underlying the therapeutic potential of ayahuasca by exploring its effects on mindfulness capacities.</td>
<td>Ayahuasca</td>
<td>1 dose (alkaloids measured) administered in a non-religious setting with experimenters present throughout session.</td>
<td>Post (24 h)</td>
<td>FFMQ</td>
<td>Statistically significant increases in scores on: Non-judgemental inner experience (P = 0.010) Non-reactivity (P = 0.034)</td>
</tr>
<tr>
<td>Thomas et al. (2013)</td>
<td>Pre/post/ follow-up Uncontrolled</td>
<td>Addiction and stress</td>
<td>None</td>
<td>n = 12 (n = 4 completed two ayahuasca retreats, n = 8 completed one retreat) Follow up: n = 11</td>
<td>Ayahuasca-naive Canadian First Nations and Aboriginal peoples Age (m = 43 based on 7 reported ages)</td>
<td>To assess the impact that ayahuasca-assisted group therapy may have on measures of mental and behavioural health related to addiction.</td>
<td>Ayahuasca, sweat lodge, spirit baths, group counselling</td>
<td>2 doses (50–100 ml) were administered by an ayahuasca ceremony.</td>
<td>Post (Week 2), Follow-up (Months 2 to 6 total of 6 follow-ups)</td>
<td>PHLMS</td>
<td>Participating in the retreat correlated with statistically significant improvements in mindfulness over time (P = 0.041) Follow up: Significant overall improvement (P &lt; 0.05)</td>
</tr>
<tr>
<td>Uthaug et al. (2018)</td>
<td>Observational Pre/post/ follow-up intervention Uncontrolled</td>
<td>Non-clinical</td>
<td>Colombian sample and Dutch sample</td>
<td>n = 57 (Colombian = 27, Dutch = 30) Follow up: n = 31</td>
<td>Participants in pre-planned ayahuasca ceremonies were invited to join the study. Dutch sample: Sex: M = 40%, F = 60% 43.3% had no previous experience with ayahuasca Colombian sample: Sex: M = 33.3% 40.7% had no previous experience with ayahuasca</td>
<td>To assess sub-acute and long-term effects of ayahuasca on well-being and cognitive thinking style and to assess whether sub-acute and long-term effects of ayahuasca depend on the degree of ego dissolution that was experienced after consumption of ayahuasca</td>
<td>Ayahuasca</td>
<td>One dose was administered by trained shaman or ayahuasca in a ceremonial setting. Four samples were assessed for alkaloid concentrations.</td>
<td>Post (1 day), Follow-up (4 weeks)</td>
<td>FFMQ</td>
<td>Statistically significant increases in scores on: Observing (P = 0.018) Non-judgemental inner experience (P = 0.016) Acting with awareness (P = 0.006) Non-reactivity (P = 0.038)</td>
</tr>
<tr>
<td>Uthaug et al. (2019)</td>
<td>Observational pre/post intervention Uncontrolled</td>
<td>Non-clinical</td>
<td>None</td>
<td>n = 42 (Mixture of three settings: Czech Republic, Spain, The Netherlands)</td>
<td>Recruited from pre-planned sessions. Sex: M = 60% F = 40% Age: m = 38 (SD 0.8)</td>
<td>To assess whether inhaling vapor containing 5-MeO-DMT produces any sub-acute and/or long lasting improvements in 5-MeO-DMT from vapor of dried toad secretions</td>
<td>5-MeO-DMT</td>
<td>Doses were administered by facilitators in non-clinical setting. Precise doses unknown, estimated between</td>
<td>Post (within 24 h), Follow-up (4 weeks)</td>
<td>FFMQ-15</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Condition</th>
<th>Control/ Subgroups</th>
<th>Sample size</th>
<th>Participants</th>
<th>Aims of study</th>
<th>Intervention/ Additional Intervention</th>
<th>How many doses/ administered by whom?</th>
<th>Time-frame (Post and Follow-up)</th>
<th>Mindfulness Outcome Measure</th>
<th>Mindfulness Results</th>
<th>Quality rating</th>
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<td>Uthaug et al. (2020)</td>
<td>Observational pre/post intervention</td>
<td>Non-clinical</td>
<td>None</td>
<td>n = 11</td>
<td>Follow up n = 10</td>
<td>Recruited after signing up for a session. Sex: M = 8 F = 3 Age: m = 33 (SD 8.59) All had previous psychedelic experience.</td>
<td>To assess the effects of 5-MeO-DMT on depression, anxiety, stress, mindfulness, and satisfaction with life.</td>
<td>Synthetic 5-MeO-DMT</td>
<td>Administered one-on-one by a facilitator in a non-clinical setting. Participants given between 1 and 4 doses varying from 17 to 61 mg total.</td>
<td>Post (immediately after session), Follow-up (7 days)</td>
<td>FFMQ</td>
<td>Main effects of session reached significance on Non-judgemental inner experience (P = 0.001) Baseline to post-session measures showed significant increase in Non-judgemental inner experience (P = 0.017)</td>
</tr>
</tbody>
</table>

Follow-up: n = 24

measures of affect and cognition. If so, whether these were related to certain aspects of the acute psychedelic state.

20 and 120 mg dried toad secretion.

Act with Awareness

Sub-acute assessments of mindfulness did not significantly differ from baseline.

Follow up: Improvements compared to baseline in Non-judgemental inner experience (P = 0.046)

Act with Awareness

Recruited after signing up for a session.

Sex: M = 8 F = 3 Age: m = 33 (SD 8.59) All had previous psychedelic experience.

To assess the effects of 5-MeO-DMT on depression, anxiety, stress, mindfulness, and satisfaction with life.

Synthetic 5-MeO-DMT

Administered one-on-one by a facilitator in a non-clinical setting. Participants given between 1 and 4 doses varying from 17 to 61 mg total.

Post (immediately after session), Follow-up (7 days)

FFMQ

Main effects of session reached significance on Non-judgemental inner experience (P = 0.001) Baseline to post-session measures showed significant increase in Non-judgemental inner experience (P = 0.017).

FFMQ = Five Facets of Mindfulness Questionnaire, PHLMS = Philadelphia Mindfulness Scale, μg = microgram, g = grams, MAAS = Mindful Attention Awareness Scale, TMS = Toronto Mindfulness Scale, FMI = Freiburg Mindfulness Inventory, 5-MeO-DMT = 5-methoxy-N,N-dimethyltryptamine.

NA = not applicable, n = Number of participants, M = Male, F = Female, m = Mean, SD = Standard Deviation, r = Range, BPD = Borderline Personality Disorder, ω² = Partial eta squared (effect size), FFMQ = Five Facets of Mindfulness Questionnaire, PHLMS = Philadelphia Mindfulness Scale, μg = microgram, g = grams, MAAS = Mindful Attention Awareness Scale, TMS = Toronto Mindfulness Scale, FMI = Freiburg Mindfulness Inventory, 5-MeO-DMT = 5-methoxy-N,N-dimethyltryptamine.
Mian et al., 2019; Thomas et al., 2013; Uthaug et al., 2018). Measuring the dose and levels of alkaloids in ayahuasca samples, as done in (Soler et al., 2016, 2018; Uthaug et al., 2018), was valuable in helping to understand dose-related effects and ensuring a standardised intervention across study populations.

With no control groups, small sample sizes, and inconsistencies in delivery of interventions, it is difficult to apply certainty in the sum of these studies’ findings. They provide a preliminary base for future research to further explore mindfulness with more methodological rigour, although it may not be possible to conform to some aspects of rigorous study design due to the way settings and interpersonal interactions are used to facilitate an individual’s experience of ingesting psychedelics.

Description of mindfulness outcome measures used and psychedelic intervention

Nine of the thirteen studies used the FFMQ to measure mindfulness (Domínguez-Clavé et al., 2019; Mian et al., 2019; Sampedro et al., 2017; Soler et al., 2016, 2018; Uthaug et al., 2018), three of which used the FFMQ-Short Form (Baer et al., 2006). Two studies used the Mindful Attention Awareness Scale (Madsen et al., 2020; Polito & Stevenson, 2019) and one used the PMA (Thomas et al., 2013). One study utilised two mindfulness measures in the Freiburg Mindfulness Inventory and the Toronto Mindfulness Scale (Smigielski et al., 2019).

The psychedelic interventions across studies varied in substance, dose, frequency, and setting. Six studies observed the effects of ayahuasca and 5-MeO-DMT administered in a ceremonial setting by experienced facilitators (Domínguez-Clavé et al., 2019; Murphy-Beiner & Soar, 2020; Thomas et al., 2013; Uthaug et al., 2018, 2019, 2020), five administered ayahuasca or psilocybin by researchers in a lay setting (Madsen et al., 2020; Sampedro et al., 2017; Smigielski et al., 2019; Soler et al., 2016, 2018), and one study observed the effects of self-administered serotonergic psychedelics (Polito & Stevenson, 2019). Mian et al. (2019) did not report ayahuasca ingestion method, setting or dose. Ten studies used a standardised number of doses per participant, whereas the number of doses per participant varied in Domínguez-Clavé et al. (2019) and Uthaug et al. (2020). The quantity of each dose, however, was pre-planned only in Madsen et al. (2020) and Smigielski et al. (2019). Otherwise doses were given according to the facilitator or researcher’s judgement taking into account the participant’s characteristics and acute experience. Self-administered psychedelics (Polito & Stevenson, 2019) were taken in a dose considered to be sub-threshold (minimal identifiable acute effects).

Impact of psychedelics on mindfulness

All but one study (Polito & Stevenson, 2019) reported a significant level of improvement in one or more mindfulness domains either sub-acute, acute, or at follow-up. Interestingly, Smigielski et al. (2019) found that trait mindfulness was significantly higher post-retreat but that state mindfulness was not significantly increased. Three studies reported an overall increase in mindfulness following ayahuasca ingestion (Madsen et al., 2020; Mian et al., 2019; Thomas et al., 2013), measured using PHLMS, FFMQ, and Mindful Attention Awareness Scale (MAAS) respectively.

Thomas et al. (2013), using the PHLMS, reported an increase in mindfulness after a short retreat during which participants participated in a number of interventions alongside the ayahuasca ceremony (which was facilitated by an experienced ayahuascero). One of the additional interventions during the retreat was group counselling sessions, part of the aim of which was to enhance present moment awareness and acceptance, the two outcomes measured by the PHLMS. This is a possible additional factor for increasing mindfulness in their study.

Seven studies showed a significant increase in scores on the FFMQ non-judgemental inner experience domain (Domínguez-Clavé et al., 2019; Sampedro et al., 2017; Soler et al., 2016, 2018; Uthaug et al., 2018). Four of these studies included participants with no previous experience of ayahuasca or 5-MeO-DMT. Sampedro et al. (2017) reported sustained significant increases on non-judgemental inner experience scores 24 h post intervention and at follow up, two months later, Uthaug et al. (2019) reported significant increases on non-judgemental inner experience scores at one month but not sub-acute (within 24 h), and Uthaug et al. (2020) reported sustained significant increases up to seven days post intervention.

The non-judgemental inner experience domain was found to be higher in individuals with meditation experience (Baer et al., 2006), potentially augmenting the perceived effects of psychedelics, however (Soler et al., 2018), included a comparison group that underwent a mindfulness training course and found that scores in the non-judgemental inner experience domain increased after ayahuasca intake independent of mindfulness training.

Five studies found a statistically significant increase in scores on the non-reactivity domain (Domínguez-Clavé et al., 2019; Murphy-Beiner & Soar, 2020; Sampedro et al., 2017; Soler et al., 2016; Uthaug et al., 2018). The non-reactivity domain is related to the non-judgemental inner experience domain in that according to a bi-dimensional definition of mindfulness (Bishop et al., 2006), they measure the ‘acceptance’ dimension.

Three studies showed a significant increase in scores on the FFMQ observation domain (Domínguez-Clavé et al., 2019; Murphy-Beiner & Soar, 2020; Uthaug et al., 2018), which measures an individual noticing internal and external experiences. These three studies also showed a significant increase in scores on the FFMQ acting with awareness domain, which measures one’s ability to focus on the present activity. All of these studies recruited participants from pre-planned ayahuasca ceremonies, facilitated by a trained ayahuascero or shaman. Domínguez-Clavé’s participants received hourly doses while Uthaug’s received one dose. Both the observation and acting with awareness domains are measuring facets of the ‘attention’ dimension of mindfulness as opposed to ‘acceptance’.
The only study which reported an increase in the description facet of mindfulness, which relates to one’s ability to describe their inner experience, was Murphy-Beiner and Soar (2020). Baer et al. (2006) suggest that the description facet is helpful in understanding individual’s mindfulness in relation to emotional intelligence and understanding and describing one’s own emotions.

Meta-analysis results

An exploratory meta-analysis (Anello & Fleiss, 1995) was completed for six of the studies (Dominguez-Clavé et al., 2019; Sampedro et al., 2017; Soler et al., 2016, 2018; Uthaug et al., 2018), all of which were of a pre-post study design, used ayahuasca and included complete subdomain scores for the FFMQ outcome measure. See Appendix 2 Table A2 for extracted data for meta-analysis.

Figure 2 shows results of subgroup meta-analysis for mindfulness facets pre and post ayahuasca ingestion. The acting with awareness and non-reactivity facets showed no significant heterogeneity or varying effects. Both of these facets showed small but significant overall effect sizes in favour of a positive ayahuasca effect. Non-judgemental inner experience and description facets reported no significant heterogeneity but prediction intervals suggest that these facets showed varying effects. Only the non-judgemental inner experience facet also showed small but significant overall effect size in favour of a positive ayahuasca effect. Only the observation facet has a significant medium level of heterogeneity, displayed varying effects based on prediction intervals and no significant overall effect.

DISCUSSION

The results of this review indicate that psychedelics may be associated with an increase in scores on mindfulness outcome measures. The overall synthesis of evidence shows a tendency toward increases in mindfulness after psychedelic ingestion over all sub-domains of mindfulness as subdivided by the FFMQ (acting with awareness, non-judgemental inner experience, non-reactivity, observation), with the exception of the description domain, which was only found to increase in one study (Murphy-Beiner & Soar, 2020).

The meta-analysis (N = 6) results indicated that in relation to ayahuasca ingestion there was an increase in scores on the acting with awareness domain, albeit with relatively wide confidence intervals across studies. Acting with awareness, along with the non-judgemental inner experience and non-reactivity domains, have previously been shown to have incremental validity in the detection of psychological symptoms (Baer et al., 2006). These three domains showed overall increases, which suggests that the increase in mindfulness after ayahuasca intake may be particularly helpful with challenges relating to self-judgmental thoughts, impulsive reactivity, or mind-wandering/distractibility. Further, increased mindfulness may aid in the ability to maintain perspective when in heightened emotional states, expressed as forms of acceptance through non-reactivity and non-judgemental inner experience.

Dominguez-Clavé et al. (2019) suggest that a more reflective approach to difficult thoughts, emotions, and situations, rather than an emotionally-driven approach, may account for increases on the non-reactivity and non-judgemental inner experience domains of mindfulness, potentially allowing an individual to have clearer perspective on a given situation. Baer et al. (2006), in the development of the FFMQ, suggested that non-judgemental inner experience (refraining from self-criticism) and non-reactivity (refraining from impulsive action) are ways of operationalising acceptance. Increasing acceptance is an established method of supporting clinical populations, notably used within ACT (Hayes et al., 2006). The significant increase in non-judgemental inner experience and non-reactivity domains observed in this systematic review, indicate that psychedelics (particularly ayahuasca) could be an effective method of improving these acceptance domains.

Additionally, Sampedro et al. (2017), Uthaug et al. (2019), and Uthaug et al. (2020) reported significant increases on the non-judgemental inner experience domain two months, one month, and seven days, respectively, after baseline. Sampedro et al. (2017) noted that scores were higher than those reported for meditators (Soler et al., 2014), which gives credence to the findings that ingestion of ayahuasca could be as effective at achieving increases in nonjudging mindfulness than a targeted meditation practice, with lasting effect. Similarly, Śmigielski et al. (2019) found that experienced meditators that received psilocybin showed significantly increased trait mindfulness post-retreat compared to those that received a placebo. It was also observed that there were significant increases in scores on the non-judgemental inner experience and non-reactivity domains after ingesting ayahuasca; with greater increases compared to meditators (Soler et al., 2016, 2018). Characteristics of non-judgemental processes have been shown to associate with lower anxiety and depression symptoms (Brown, Bravo, Roos, & Pearson, 2015). Therefore future interventions utilising psychedelics interventions may benefit from targeting specific elements of mindfulness, such as those relating to acceptance.

Observation, acting with awareness, and description domains have been thought to measure more attentional components of mindfulness (Baer et al., 2006). Significant increases on scores on observation, acting with awareness, and description domains were found in only three of the nine studies that used the FFMQ, which utilised ayahuasca or 5-MeO-DMT from dried toad secretion vapor. This may show that the overall effects of psychedelics in these studies are more related to openness and attention (i.e. characteristics of the observation, acting with awareness, and description domains) than acceptance. However, further research would be important to explore the overlap and difference between openness, acceptance and attention. Dominguez-Clavé et al. (2019), Murphy-Beiner and Soar (2020), and Uthaug et al. (2018) measured statistically significant increases on the observation domain.
Fig. 2. Forest Plot of pre and post ayahuasca ingestion in relation to 5 facets of mindfulness. 95% CI = 95% Confidence Intervals. $I^2$ = heterogeneity. SMD = Standardised Mean Difference.
Domínguez-Clavé et al. (2019) suggest that increases on this domain could lead to greater connectedness with the present moment, which is a strategy used in many mindfulness-based therapies such as ACT, DBT or MBSR (Hayes et al., 2006; Kabat-Zinn, 1990; Linehan, 1993). A combinatory psychedelic-assisted mindfulness therapy, particularly using psilocybin, has been found to have potential positive effects on managing depression and anxiety, as well as suggesting complementary or shared neurobiological and neurocognitive mechanisms (Elefteriou & Thomas, 2021; Felsch & Kuypers, 2022; Heuschkel & Kuypers, 2020). As such, psychedelics-assisted therapies and psychological therapies (such as MBSR) may have complementary mechanisms of action that, when working in parallel, could improve outcomes relating to wellbeing, quality of life, acceptance and compassion. However, this area would benefit from future research.

Thomas et al. (2013) measured an overall increase in mindfulness using the PHLMS. They suggested that this increase in mindfulness, more specifically, self-acceptance, could contribute to the positive therapeutic effects of ayahuasca. Mian et al. (2019) found that individuals report an overall increase in mindfulness after an ayahuasca session. The two included studies to use psilocybin specifically, Smigielski et al. (2019) and Madsen et al. (2020), found an overall increase in mindfulness post-intervention. Both found an increase in trait mindfulness using the Freiburg Mindfulness Inventory (FMI), and MAAS, but Smigielski et al. (2019) found that changes in state mindfulness due to psilocybin, measured using the Toronto Mindfulness Scale (TMS), did not significantly increase.

The fair quality of included studies overall resulted in a reduced ability to generalise the results to a wider population. There are, however, a number of methodological improvements that could be made to future research. Using well characterised intervention and control group within the study design would help to minimise the effect of outside variables. Standardisation of mindfulness outcome measures or constructs measured would help in harmonising findings of future research and add evidence to this developing area of research.

Overall, an increase in randomised controlled studies and prospective cohort studies would be valuable in exploring causal relationships between psychedelics and mindfulness. Ayahuasca in particular presents a challenge to researchers in that the ceremony is often an integral part of the therapeutic process. However, controlling the environment will inevitably alter some individualised aspects of the session, thereby potentially reducing or changing the effect of the ayahuasca session. This further suggests that more research studying environmental factors may aid in understanding the fuller picture of an ayahuasca session and its therapeutic value. Pre-determined doses of the chosen psychedelic from a single batch would allow the possibility of controlling for dose-related differences (Riba et al., 2001).

Finally, the importance of set and setting (Eisner, 1997) and the resulting differences in experience highlights the need for detailed descriptions of the intervention including any pre-education, dose and concentration of psychedelic, additional elements such as a shaman, music, dietary preparation, and post-session integration of the experience. Further, the timeframe of assessing mindfulness-related outcomes following psychedelic ingestion was found to be variable, particularly in relation to longer term follow-up. Therefore, consensus and standardisation of timeframe, as well as set and setting, for psychedelic-assisted therapy in the context of mindfulness would be beneficial for future development of this research area (i.e. future trials) and practical transferability.

There are some limitations to this systematic review. By focusing on mindfulness outcome measures specifically, e.g. FFMQ, PHLMS, others were not discussed but may have been measuring an aspect of mindfulness, e.g. MINDSENS composite index (Soler et al., 2014) and Experience Questionnaire (Fresco et al., 2007). Further, there is possibility of publication bias, which has the potential to skew effect sizes and artificially favour positive outcomes (Joober, Schmitz, Annable, & Boksa, 2012). In the sub-group meta-analysis, there were a relatively small number of studies with small sample sizes included. This could have affected the estimation of heterogeneity of studies, effect sizes, and confidence intervals. The heterogeneity of studies might be indicative of the variability in treatment non-specific (e.g. time, attention, expectations, placebo effects, facilitator experience) and specific (e.g. set/preparation, setting, dose) factors related to use of psychedelics in research. Future research should further examine these factors, so as to improve robustness of future psychedelic (and mindfulness) studies. Further, many of the studies included do not contain a comparator control group and therefore should be interpreted with consideration of this, there might be individual differences (e.g. trait mindfulness) driving any significant findings. Future research could look at comparison of psychedelic users to non-using controls in relation mindfulness measures, to ensure methodological robustness and validity of results. As more controlled studies are conducted using psychedelics that also include mindfulness measures, it will provide opportunities to explore the interplay of these treatment factors, as well as if any effects are observed over long-term follow ups, across clinical and non-clinical populations.

CONCLUSION

This systematic review and meta-analysis showed an increase in mindfulness relative to ingestion of psychedelics. Mindfulness facets relating to acceptance (non-judgemental inner experience and non-reactivity) seem to be affected, along with certain elements relating to attention (acting with awareness). However, further high-quality research is needed to elucidate the relationship between mindfulness and its facets relative to psychedelic ingestion.

Conflict of interest: The authors report no conflict of interest.
REFERENCES


## Appendix 1

### Table A1. Quality ratings for all included studies (N = 13)

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality Assessment Tool</th>
<th>Quality</th>
<th>Objective clearly stated?</th>
<th>Eligibility criteria described?</th>
<th>Representative participant?</th>
<th>All eligible participants enrolled?</th>
<th>Sample size sufficiently large?</th>
<th>Intervention clearly described and delivered?</th>
<th>Outcome measures prespecified/consistent?</th>
<th>Blinded assessors?</th>
<th>Loss to follow-up &lt;20%?</th>
<th>Statistical tests for pre/post intervention?</th>
<th>Randomized comparison groups?</th>
<th>Intention to treat analysis used?</th>
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<tbody>
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<td>Before-After (Pre-Post) Studies With No Control Group</td>
<td>Fair</td>
<td>Yes</td>
<td>CD</td>
<td>CD</td>
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NA = Not applicable, NR = Not reported, CD = Cannot determine
### Table A2. Quantitative data extracted from studies for meta-analysis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Mindfulness Measure/Subgroup</th>
<th>Mean (pre)</th>
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<th>Mean (post)</th>
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SD = standard deviation, n = number of participants, BPD = Borderline Personality Disorder, FFMQ = Five Facets of Mindfulness Questionnaire.
† Different scoring criteria used.