The use of psychedelic agents in the treatment of alcohol and tobacco dependence: An integrative review

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Objective: to analyze studies that address the use of psychedelic agents in the treatment of alcohol and tobacco dependence in the national and international contexts.


Results: the final sample totaled 14 articles that addressed the use of psychedelic agents in the treatment of alcohol and tobacco dependence in the national and international contexts. Conclusion: the use of psychedelic agents in the treatment of alcohol and tobacco dependence may not be conclusive in the treatment of chemical dependence as a single therapy; however, its use can be an effective innovation to the current treatment models, so that this includes the patient’s psychedelic experience and its relationship with treatment.

Descriptors: Hallucinogens; Treatment; Chemical Dependence; Alcoholism; Tobacco Use Disorder.
O uso de agentes psicodélicos no tratamento da dependência de álcool e tabaco: revisão integrativa

Objetivo: analisar os estudos que abordam o uso de agentes psicodélicos no tratamento da dependência de álcool e tabaco no contexto nacional e internacional. Método: revisão integrativa na Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), Medical Literature Analysis and Retrieval System Online (Medline), Scientific Eletronic Library Online (SciELO), EBSCO e PubMed, utilizando-se os descritores: "Alucinógenos", "Dependência Química", "Tratamento", "Alcoolismo", "Tabagismo", "Hallucinogens", "Chemical Dependence", "Treatment", "Alcoholism", "Tobacco Use Disorder". Resultados: a amostra final totalizou 14 artigos, que abordaram o uso de agentes psicodélicos no tratamento de dependência de álcool e tabaco, no contexto nacional e internacional. Conclusão: o uso de agentes psicodélicos no tratamento da dependência de álcool e tabaco, não é conclusivo no tratamento da dependência química como terapêutica única, entretanto, sua utilização pode ser uma inovação eficaz para os modelos atuais de tratamentos, de modo que engloba a experiência psicodélica do paciente e a relação desta com o tratamento.

Descritores: Alucinógenos; Terapêutica; Transtornos Relacionados ao Uso de Substâncias; Terapia; Alcoolismo; Tabagismo.

El uso de agentes psicodélicos en el tratamiento de la dependencia de alcohol y tabaco: revisión integradora

Objetivo: analizar estudios que aborden el uso de agentes psicodélicos en el tratamiento de la adicción al alcohol y al tabaco en el contexto nacional e internacional. Método: revisión integradora en Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS), Medical Literature Analysis and Retrieval System Online (Medline), Scientific Eletronic Library Online (SciELO), EBSCO y PubMed, utilizando los siguientes descriptores: "Alucinógenos", "Tratamiento", "Dependencia Química", "Alcoolismo", "Tabagismo", "Hallucinogens", "Treatment", "Chemical Dependence", "Alcoholism" y "Tobacco Use Disorder". Resultados: la muestra final consideró 14 artículos que abordaron el uso de agentes psicodélicos en el tratamiento de la adicción al alcohol y al tabaco en el contexto nacional e internacional. Conclusión: el uso de agentes psicodélicos en el tratamiento de la dependencia al alcohol y al tabaco no es concluyente en el tratamiento de la dependencia química como terapia única; sin embargo, su uso puede implicar una innovación eficaz a los modelos de tratamiento actuales, dado que incluye la experiencia psicodélica del paciente y la relación de la misma con el tratamiento.

Descritores: Alucinógenos; Tratamiento; Dependencia Química; Alcoholismo; Tabaquismo.
Introduction

The use of psychoactive substances accompanies humanity’s history and culture. In the search for pleasure, and also to heal distresses, several substances have been discovered, whether natural or artificial. However, there is a set of harmful effects that are caused when there is chemical dependence on these substances[1].

Globally, alcohol dependence is the most prevalent in the world, and harmful alcohol use is responsible for 3 million deaths a year worldwide, in addition to being a factor for more than 200 injuries and diseases[2]. In Brazil, the 2017 National Survey on Drug Use by the Brazilian Population exposes abuse and dependence on numerous substances, showing alarming data, mainly regarding the use of licit drugs such as alcohol and tobacco[3]. Tobacco kills more than seven million people every year; even though its consumption has decreased significantly since 2000, it is still insufficient to avoid the consequences of using this substance, such as cardiovascular diseases and other chronic non-communicable diseases, including 44% of all deaths[4]. If the number of consumers is high, the sample space increases, which consequently covers people pre-disposed to the development of a possible chemical dependence.

As it is a public health problem, the Brazilian State spends considerable amounts of money for the treatment of citizens who have chemical dependence[5]. Initially, dependent use of tobacco – which is one of the most prevalent in Brazil – harms the State economically by approximately 60 billion reais a year due to medical expenses for treatment, and carries with it nearly 160,000 deaths that could be avoided[6]. Smoking causes dependence, initially on nicotine, which stimulates the brain to release various neurotransmitters, inducing the body to a sense of pleasure[7].

Together, according to a survey by researchers from the Oswaldo Cruz Foundation (FIOCRUZ), the Federal University of Rio de Janeiro (Universidade Federal do Rio de Janeiro, UFRJ), the State University of Rio de Janeiro (Universidade Estadual do Rio de Janeiro, UERJ) and the Health Surveillance Secretariat of the Ministry of Health, the financial impact to treat diseases related to alcoholism by the Unified Health System (Sistema Único de Saúde, SUS) is estimated at around 8.2 million reais a year, and reaches nearly 10% of the Brazilian population[8]. Alcoholism tends to be attributed to environmental factors, such as: 1) Cultural development; 2) Economy; 4) Alcohol availability. Even if there is not only one dominant factor, the greater the vulnerability in which the individuals are in, the more likely they are to develop problems related to alcohol and its use[9]; therefore, it is remarkable that chemical dependence, especially on alcohol and tobacco, is a relevant condition for the government, in social and economic terms.

The treatment of alcoholism is based on several aspects, which are determined according to the severity of dependence, but which are distributed from Primary Health Care (PHC) to specialty centers, ranging from continuous follow-up therapies to drugs that control the alcohol withdrawal syndrome[10]. On the other hand, treatment of the smoking habit is based on nicotine replacement therapy, aiming to minimize the symptoms of the withdrawal syndrome, as well as on the use of the bupropion hydrochloride drug[11].

Due to the search for new treatments, the scientific community added to the group of therapeutic alternatives the use of psychedelic agents for the treatment of dependence on psychoactive substances[12], as an example we have psilocybin, a hallucinogenic substance found in mushrooms of the Psilocybe cubensis species, which, after scientific studies, was discovered as with therapeutic potential for the treatment of chemical dependence[13].

The scientific community has been looking at new therapeutic alternatives for alcoholics and smokers; in this sense, this research conducted a survey of bibliographic productions on the use of psychedelic agents in the treatment of alcohol and tobacco dependence in the national and international contexts. The objective was to identify and describe the treatments of the tobacco and alcohol addictions conducted with the use of psychedelic agents, aiming to assist in increasing the sampling of therapeutic alternatives.

Method

This is a study of the Integrative Literature Review type, whose methodology aims at synthesizing results obtained from a broad analysis of the literature on a given theme or question, in a systematic and orderly manner, contributing to discussions on the research methods and results[14].

Preparation of this integrative review study followed six stages: 1) Identification of the theme and selection of the research question for the elaboration of the integrative review; 2) Establishment of criteria for inclusion and exclusion of studies/sampling; 3) Definition of the information to be extracted from the studies selected, as well as categorization of the studies; 4) Evaluation of the studies included in the integrative review; 5) Interpretation of the results; and 6) Presentation of the review and synthesis of the knowledge[15]. In addition, in order to guide the integrative review, the following guiding question was elaborated: Which is the effect of psychedelic agents on the treatment of alcohol and tobacco dependence reported in the scientific production from 2010 to 2020?

The articles were searched and selected jointly in July 2020. All the articles selected were compared with each other in order to verify repetition and agreement.
The initial search included 127 articles in Scielo, 152 in LILACS, 5,314 in EBSCO, 554 in PUBMED and 1,667 in MEDLINE, totaling 7,834 articles and, after reading their titles and abstracts, only 61 articles remained. Of these, after applying the inclusion and exclusion criteria, 14 articles remained that portrayed the use of psychedelic agents in the treatment of alcohol and tobacco dependence, in the national and international contexts.

The descriptors used were defined based on the Descriptors in Health Sciences, with the following terms and their combinations, separated by the Boolean operators "AND" and "OR", in Portuguese and English: "Alucinógenos", "Dependência Química", "Tratamento", "Alcoolismo", "Tabagismo", "Hallucinogens", "Chemical Dependence", "Treatment", "Alcoholism" and "Tobacco Use Disorder", in combinations that totaled 9 different search strategies (Figure 1).

<table>
<thead>
<tr>
<th>SEARCH TERMS</th>
<th>SCIELO</th>
<th>LILACS</th>
<th>EBSCO</th>
<th>PUBMED</th>
<th>MEDLINE</th>
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<tbody>
<tr>
<td>&quot;Alucinógenos&quot; OR &quot;Agentes psicodélicos&quot;</td>
<td>37</td>
<td>25</td>
<td>373</td>
<td>7</td>
<td>312</td>
</tr>
<tr>
<td>&quot;Alucinógenos&quot; OR &quot;Agentes psicodélicos&quot; AND &quot;Tratamento&quot;</td>
<td>2</td>
<td>10</td>
<td>192</td>
<td>0</td>
<td>189</td>
</tr>
<tr>
<td>&quot;Agentes psicodélicos&quot; OR &quot;alucinógenos&quot; AND &quot;tratamento&quot; AND &quot;dependência química&quot; OR &quot;adição a drogas&quot;</td>
<td>1</td>
<td>0</td>
<td>152</td>
<td>0</td>
<td>189</td>
</tr>
<tr>
<td>&quot;Hallucinogens&quot; OR &quot;Psychedelic Agents&quot; AND &quot;treatment&quot;</td>
<td>38</td>
<td>53</td>
<td>2,113</td>
<td>304</td>
<td>325</td>
</tr>
<tr>
<td>&quot;Hallucinogens&quot; OR &quot;Psychedelic Agents&quot; AND &quot;treatment&quot; AND &quot;Chemical Dependence&quot; OR &quot;Drug addiction&quot;</td>
<td>4</td>
<td>18</td>
<td>1,594</td>
<td>189</td>
<td>98</td>
</tr>
<tr>
<td>&quot;Agentes psicodélicos&quot; OR &quot;alucinógenos&quot; AND &quot;tratamiento&quot; AND &quot;dependencia quimica&quot; OR &quot;Adicion a Drogas&quot;</td>
<td>2</td>
<td>25</td>
<td>373</td>
<td>7</td>
<td>312</td>
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<tr>
<td>&quot;Agentes psicodélicos&quot; OR &quot;alucinógenos&quot; AND &quot;tratamiento&quot;</td>
<td>2</td>
<td>5</td>
<td>348</td>
<td>0</td>
<td>189</td>
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<tr>
<td>&quot;Agentes psicodélicos&quot; OR &quot;alucinógenos&quot; AND &quot;tratamiento&quot; AND &quot;dependencia quimica&quot; OR &quot;Adicion a Drogas&quot;</td>
<td>2</td>
<td>2</td>
<td>109</td>
<td>0</td>
<td>25</td>
</tr>
</tbody>
</table>

Figure 1 - Search terms used. Palmas, TO, Brazil, 2020

The initial search included 127 articles in Scielo, 152 in LILACS, 5,314 in EBSCO, 554 in PUBMED and 1,667 in MEDLINE, totaling 7,834 articles and, after reading their titles and abstracts, only 61 articles remained. Of these, after applying the inclusion and exclusion criteria, 14 articles remained that portrayed the use of psychedelic agents in the treatment of alcohol and tobacco dependence, in the national and international contexts.

For analysis and subsequent synthesis of the articles selected, a synoptic table was used, including the following: title, author, year, database, study objective, methodology, result, analysis and conclusion.

Results

The studies were predominantly published in the period from 2014 to 2019, with only one study published in 2011. As for the origin and language of the publications, eleven articles were published in English, eight of which came from the United States, one from Canada, one from the United Kingdom and the other without identification of its locus; two articles in Portuguese from Spain, and a single article published in Spanish, in Spain.

Regarding the type of study, predominance of quantitative studies was identified, of which: seven were clinical trials and three were open pilot studies, in which two articles worked with the same study, where moderate (20 mg/70 kg) and high (30 mg/70 kg) doses of psilocybin were used in a smoking cessation treatment with 15 participants, during 15 weeks, and the other study used psilocybin for the treatment of alcohol dependence, with doses of 0.3 mg/kg and 0.4 mg/kg, in different sessions, over 12 weeks, with 10 participants; a double blind placebo-controlled treatment with psilocybin on alcohol use dependence, lasting 12 weeks; two experimental studies conducted with mice, in one, the potential of acute administration of ayahuasca and...
METHODOLOGY

COUNTRY

MAIN RESULTS

OBJECTIVE

AUTHOR (YEAR)

Qualitative research: in-depth interview.

Gomes et al. (2011) 16

Brazil

To understand the ritual use of ayahuasca in the treatment and recovery of homeless people in São Paulo.

The therapeutic effects of tea are linked to how it is understood and used by the participant.

Johnson et al. (2014) 17

USA

It illustrates a framework for future research studies about the efficacy and mechanisms of hallucinogen-facilitated treatment for addictions.

Open pilot study administering moderate (20 mg/70 kg) and high (30 mg/70 kg) doses of psilocybin.

The smoking cessation rate observed substantially exceeds those commonly reported for other behavioral and/or pharmacological therapies.

Bogenschutz et al. (2018) 18

USA

To illustrate the range of experiences and persistent effects of psilocybin treatment.

Double-blind, placebo-controlled clinical trial of psilocybin-assisted treatment of alcohol use disorder.

Descriptive case studies provide a useful window into the therapeutic process of the psychedelic treatment of addictions.

Nielsen et al. (2018) 19

USA

To explore how the patients report on change-related phenomena during post-medication debriefing sessions.

Open pilot study of psilocybin-assisted treatment for alcohol dependence with participants who met the DSM-IV-TR criteria for such dependence.

The participants articulated a series of main phenomena related to changing the outcomes of alcohol consumption and the acute subjective effects of psilocybin.

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<table>
<thead>
<tr>
<th>AUTHOR (YEAR)</th>
<th>COUNTRY</th>
<th>OBJECTIVE</th>
<th>METHODOLOGY</th>
<th>MAIN RESULTS</th>
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</thead>
<tbody>
<tr>
<td>Garcia-Romeu et al.</td>
<td>USA</td>
<td>To investigate the potential psychological mechanisms that mediate the</td>
<td>Open pilot study about the treatment of the smoking habit facilitated by</td>
<td>The smoking cessation outcomes were significantly correlated with measures</td>
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<td>(2015)</td>
<td></td>
<td>results of the psilocybin-facilitated treatment of dependence.</td>
<td>psilocybin in the context of the cognitive-behavioral therapy.</td>
<td>of mystical experience on session days.</td>
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<td>Heink et al. (2016)</td>
<td>USA</td>
<td>It adds to the literature using 5d-ASC, a psychometrically sound measure</td>
<td>The researchers collected data using an anonymous, online and retrospective</td>
<td>The results indicated a positive correlation between the several dimensions</td>
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<td></td>
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<td>of altered states of consciousness (ASCs) to examine ibogaine-induced ASCs.</td>
<td>survey.</td>
<td>of the ASCs.</td>
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<td>Johnson et al. (2017)</td>
<td>USA</td>
<td>To complement a laboratory research study on smoking cessation.</td>
<td>An anonymous survey, conducted online with a sample of 358 individuals.</td>
<td>The individual outcomes related to the smoking habit varied, including</td>
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<td></td>
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<td>total abstinence, persistent reductions in the rate of prior smoking, and</td>
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<tr>
<td>Vargas-Perez et al.</td>
<td>Canada</td>
<td>The goal is to prove that the 5-HT2A agonists can be used as therapeutic</td>
<td>Administration of non-selective 5-HT2A agonist 4-Acetoxy-Dimethyltryptamine</td>
<td>Pretreatment with a single injection of systemic 4-AcO-DMT before administration</td>
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<tr>
<td>(2017)</td>
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<td>agents to reverse a state of drug dependence, as well as inhibit the</td>
<td>(4-AcO-DMT) in chronic opioids, chronic nicotine or intra-VTA BDNF treated</td>
<td>can prevent the rewarding motivational effects of nicotine in addicted mice,</td>
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<td>Loizaga-Velder et al.</td>
<td>UK</td>
<td>aversive effects produced by drug withdrawal.</td>
<td>in previously untreated rodents.</td>
<td>blocking withdrawal aversion.</td>
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<td>(2014)</td>
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<td>Talin et al. (2017)</td>
<td></td>
<td>To examine people’s healing experiences, that is, their attempts to</td>
<td>A qualitative and ethnographically-based analysis of addiction recovery</td>
<td>The efficacy of ayahuasca in treating dependence mixes the somatic, symbolic</td>
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<td></td>
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<td>cure substance use they find problematic.</td>
<td>experiences in ayahuasca rituals.</td>
<td>and collective dimensions.</td>
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<td>Vitor (2019)</td>
<td>Brazil</td>
<td>To evaluate the potential of Ayahuasca (AYA) to prevent the expression</td>
<td>The influence of acute administration of AYA (1.76, 3.0, 17.6 and 30.0 mg/kg</td>
<td>Analytical characterization of the drugs and behavioral analysis were</td>
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<td>of behavioral sensitization induced by cocaine and the neurochemical</td>
<td>of DMT o.r.) on the locomotor activity of the animals (mice) in the open</td>
<td>performed. The results suggest that AYA can be a good therapeutic strategy</td>
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<td>Apud (2019)</td>
<td>Spain</td>
<td>To describe and analyze the processes of cure of dependence cases treated</td>
<td>field was evaluated.</td>
<td>for cocaine addiction, paving the way for new studies.</td>
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<td>at the Amazon Institute of Applied Ethnopsychology (Instituto de</td>
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<td>Ethnopsiología Aplicada da Amazônia, IDEAA).</td>
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**Figure 2** – Synthesis for the articles selected. Palmas, Tocantins, Brazil, 2020
Discussion

Dependence on alcohol and nicotine are considered chronic disorders that disturb the individuals’ psychological and physiological systems, in which they use these substances to generate comfort or alleviate symptoms caused by withdrawal\(^{(20)}\). Dependence disorders involve a complex neuromodulation process in which these substances alter cellular and molecular aspects of the neurological function, which generate compulsive behavioral effects, but are also influenced by genetic, psychological, social and environmental factors\(^{(1)}\).

The pharmacological approach is an important factor in the treatment of alcohol and tobacco dependence, in parallel with the psychological intervention, and the social approach. In general, drugs are used in replacement, detoxification and prevention of relapses\(^{(1)}\). The advances in psychopharmacology in the treatment of substance abuse disorders benefited a large number of people; however, due to delay in treatment and to the presentation of several side effects, the pharmacological therapy currently used presents limited effectiveness, as there is low adherence to the use of the medications and/or withdrawal of the recommended therapy\(^{(21)}\).

A promising treatment model is being studied as a complementary therapeutic alternative in a renaissance of research studies on psychedelic substances\(^{(17-18)}\). In studies using psilocybin, the mysticomimetic experience can explain some aspects of the positive results of the patient’s integration, being a considerable promise in promoting long-term smoking abstinence\(^{(20)}\).

Other studies indicate that the rituals of the consumer community of ayahuasca, together with social integration, can assist in the treatment of chemical dependence, constituting fluid and adaptable care modalities that play a fundamental role in treatment success, as feeling part of a community has an important therapeutic potential\(^{(27)}\).

Studies based on experimental and virtual research show self-reported reductions in alcohol and tobacco consumption, some determined by international scores\(^{(20-21)}\).

The ritualistic approach with ayahuasca allowed describing the effects in helping to treat dependence. In the first place, the experience is broader than the mere ritualistic process. The patients need to be integrated into the psychedelic experience, to create interactions that produce a memory of this experience; then, the patients’ psychedelic experience will be interpreted and re-signified so that, with this, they can establish a link between their new memories, brought by the ritualistic process, and the old memories already existing\(^{(29)}\).

Studies showing empirical hypotheses with attempts to explain the pharmacodynamics of psychedelic agents were also found\(^{(25-26,28)}\). The partially accepted hypothesis shows the functionalities of ibogaine. Using 5d-ASCs, a psychometrically sound measure of altered states of consciousness (ASCs), it is remarkable that there is a positive correlation between the several dimensions of the ASCs and the patient’s improvement, explained by an ability of the ibogaine therapy to provoke changes in the patient’s life and desires\(^{(22)}\).

Conclusion

The use of psychotropic drugs in the treatment of alcohol and tobacco dependence is not conclusive for the effective treatment of such dependence; however, the use of these entheogenic agents, according to the studies analyzed, shows a window of possibility for an innovation in the current treatments, so that this encompasses the patients’ psychedelic experience, their interaction and co-participation in the treatment.

It was evident in the studies addressed that the experience itself, provided by the psychedelic agents, is broad, and that its therapeutic management needs to include integration activities that contribute to treatment innovation. Another important element is the creation of a memory of the experience with psychedelic agents, which is interpreted and re-signified, so that, from a biographical point of view, it becomes the key articulation point between an old and a new personality.

It was also observed that mystical-mimetic experiences are perceived as a relevant contribution to the treatments. Some patients report, and scientific scales confirm, very intense individual experiences similar to mystical states, which produce a sense of well-being and personal growth.

This study sought to collaborate with the systematization of knowledge on the theme, stimulating further discussions on the use of psychedelic agents in the treatment of alcohol and tobacco dependence, in order to help expand treatment perspectives, as well as show new contributions to the therapeutic methods.

References


Authors’ contribution


All authors approved the final version of the text.

Conflict of interest: the authors have declared that there is no conflict of interest.