

A conceptual analysis and systematic literature review on the role of *Chavyadi Churna* in Alcohol use disorder associated anxiety

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Abstract

Alcohol dependence is a significant global health concern, leading to substantial morbidity and mortality. Anxiety disorders commonly coexist with Alcohol Use Disorder (AUD), increasing the risk of relapse. Conventional treatments prioritize abstinence but often overlook AUD-related anxiety. This study explores the potential of *Chavyadi Churna*, an Ayurvedic herbal formulation from Bhela Samhita, as an anxiolytic remedy for AUD-induced anxiety. A systematic literature review was conducted following PRISMA 2020 guidelines. Studies were sourced from PubMed, Scopus, and Google Scholar, focusing on the anxiolytic properties of herbal formulations in the context of alcohol dependence. Only peer-reviewed studies from the last decade were included. A conceptual analysis was performed using an empirical development approach. The research evaluated the bioactive components of *Chavyadi Churna* and their pharmacological effects on anxiety related to AUD. Findings were synthesized using AMSTAR criteria to ensure a high standard of evidence synthesis. Modern pharmacological treatments for AUD-associated anxiety primarily target serotonin reuptake and GABAergic modulation. *Chavyadi Churna* comprises herbs such as *Piper chaba* Trel. and Yunck, *Ferula asafoetida* L, *Citrus medica* L, *Zingiber officinale* Roscoe, and *Apium graveolens* L. known for their neuroprotective and calming effects. These ingredients may help restore neurotransmitter balance, reduce oxidative stress, and mitigate the physiological consequences of chronic alcohol consumption. *Chavyadi Churna* shows promise as a complementary therapy for managing AUD-related anxiety.

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Substance abuse is a critical health care issue today. The WHO Global Status Report on Alcohol and Health 2024 highlights that alcohol is responsible for an estimated 3.3 million deaths annually and 5.1% of global Disability Adjusted Life Years, emphasizing the need for effective interventions.²¹ Alcohol use is a significant modifiable risk factor for non-communicable diseases.²⁰ The National Household Survey of Drug Use in India documented that alcohol is the primary substance used by 21.4% of the population, with 17-26% of these users meeting the ICD-10 criteria for dependence¹⁵. Alcohol dependence is a complex condition involving biological, psychological, and social factors. In India, anxiety disorders are prevalent among alcohol-dependent individuals, particularly those from lower socio-economic backgrounds, those who are separated from their spouses, and those who are unemployed. Anxiety also significantly contributes to the likelihood of relapse in individuals treated for alcohol dependence. Research indicates that 23-70% of patients in alcohol treatment programs also have anxiety disorders, and 20-45% of people with anxiety disorders have a history of alcoholism. Therefore, addressing co-occurring anxiety disorders is essential for successful alcohol treatment, necessitating a combined approach to managing both conditions¹³. The relationship between alcoholism and *Panatyaya*, a condition characterized by numbness, pain, and cardiovascular disturbances, can be understood through both pharmacological and Ayurvedic perspectives. Chronic alcoholism leads to central nervous system depression and

neurotransmitter imbalance, contributing to *Panatyaya* symptoms¹⁵. Ayurveda links these symptoms to a *Vata* imbalance, which is exacerbated by alcohol's properties. The treatment focuses on restoring *Vata* balance through detoxification, herbal remedies, and lifestyle changes. Understanding and addressing both the physiological and psychological effects of alcohol, along with traditional Ayurvedic practices, is crucial in developing holistic treatment strategies for alcohol dependence and related anxiety keeping in view the symptomatic treatment of anxiety in modern medicine. The treatment of anxiety is thus, a vital component in managing alcoholism effectively. *Chavyadi Churna* is a formulation prescribed by *Bhela Samhita*, *Chikitsa Sthana*, *Panatyaya Chikitsa*, as a deaddiction measure to be administered along with alcohol⁹. There are no research works done on this formulation from preclinical or clinical aspect till date. This paper is thus, an attempt to conceptually analyse the potential of *Chavyadi Churna* as an anxiolytic medication in AUD associated anxiety.

Empirical development was adopted for conceptual analysis in the current paper. This methodology helps in bridging the gap between theoretical concepts and real-world data by thoroughly reviewing existing literature, collection of data, analysis of data to identify patterns leading to validation of the concept. The eligibility criteria for the systematic literature search adopted in the present paper included research works done on the individual ingredients of *Chavyadi Churna* from the perspective of anxiolytic activity in alcohol

dependency. The search started from a broader perspective on previous researches done on *Chavyadi Churna* to know the status of knowledge and was later narrowed down to the probable mechanism and activity of individual herbal drugs in *Chavyadi Churna* with special reference to alcohol dependency and associated anxiety. Databases searched included PubMed, Scopus and Google Scholar. Alcohol Use Disorder, Anxiety, Anxiolytic, Alcohol dependency were the keywords used along with 'AND' as the Boolean operator. Research papers on individual ingredients were done by combining the botanical names with the above-mentioned keywords. Publications which have been published within the last 10 years and full papers of which were available were only considered for the review. The literature search was performed according to the PRISMA guidelines 2020. The titles and abstracts of the research

papers were initially screened followed by screening based on content. RoB 2 of Cochrane Collaboration's Tool for Assessing Risk of Bias was used for RCTs for assessment of risk of bias. Results of the literature search have been reported according to AMSTAR guidelines. Since, the literature search and subsequent review didn't involve systematic review of research works limited to either human studies or experimental animal studies, the review article was not registered in PROSPERO.

A total of 15 articles which included research works done on individual drugs of interest with reference to *Chavyadi Churna* were reviewed. The PRISMA flowchart giving the number of records reviewed and the search strategy illustrates the literature search process (Figure 1).

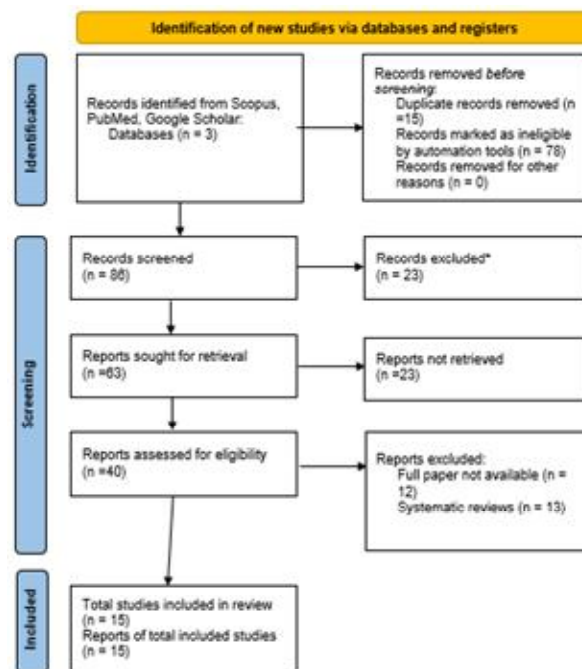


Figure 1. PRISMA Flowchart.

The review was done on a total of 15 research papers which included 7 *in vitro* studies and 8 clinical trials. The PICO characteristics of the reviewed papers has been tabulated in Table 1. The risk of bias assessment has been visualised using robvis tool as illustrated as a summary plot in Figure 2.

Table-1. PICO Characteristics of reviewed papers.

Author	Population	Intervention	Comparator	Outcome
Farchione <i>et al.</i> (2021)	Individuals with comorbid alcohol use and anxiety disorders.	Unified Protocol for the treatment of comorbid alcohol use and anxiety	Not specified	Efficacy of the Unified Protocol in treating comorbid alcohol use and anxiety disorders.
Wolitzky-Taylor <i>et al.</i> (2015)	Individuals with anxiety disorders in a primary care setting.	Anxiety treatment outcomes.	Different levels of alcohol use severity.	Impact of alcohol use severity on anxiety treatment outcomes.
Randall, Thomas, and Thevos (2001)	Individuals with concurrent alcoholism and social anxiety disorder.	Developing effective treatments for concurrent alcoholism and social anxiety disorder.	Not specified	First step toward developing effective treatments.
Anker <i>et al.</i> (2016)	Patients with co-occurring alcohol use disorder and anxiety disorder.	Treatment for alcohol use disorder.	Different levels of drinking to cope with negative emotions.	Moderation of treatment response by drinking to cope with negative emotions.
Lee <i>et al.</i> , ¹⁰ Hwang JS, Oh GJ, Lee KS (2005)	<i>In vitro</i> study	Piperine from <i>Piper longum</i>	Not specified	Inhibitory effect on monoamine oxidase and antidepressant-like activity.
Costa <i>et al.</i> , ⁴	<i>In vitro</i> study	<i>Citrus aurantium</i> L. essential oil.	Not specified.	Anxiolytic-like activity mediated by 5-HT _{1A} -receptors and reduced cholesterol

				after repeated oral treatment.
Haque <i>et al.</i> , ⁷	<i>In vitro</i> study	<i>Piper chaba</i> Hunter.	Not specified.	Review of phytochemical and pharmacological properties.
Dehpour <i>et al.</i> , ⁵	<i>In vitro</i> study	Methanol extract of <i>Ferula assaf-oetida</i> and its essential oil.	Not specified	Antioxidant acitivity
Costa <i>et al.</i> , ⁴	<i>In vitro</i> study	<i>Citrus aurantium</i> L. essential oil.	Not specified	Anxiolytic-like activity mediated by 5-HT1A-receptors and reduced cholesterol after repeated oral treatment.
Mao <i>et al.</i> , ¹¹	<i>In vitro</i> study	Ginger (<i>Zingiber officinale</i> Roscoe).	Not specified	Bioactive compounds and bioactivities.
Mehraj and Alam ¹²	<i>In vitro</i> study	Karafs (<i>Apium graveolens</i> Linn).	Not specified	Historical context, therapeutic properties, ethnopharmacological applications, and scientific research.
Nigam ¹⁴	Individuals experiencing stress, anxiety, and depression.	Alcohol consumption.	Not specified	Understanding the relationship between alcohol consumption and stress, anxiety, and depression.
Smith and Randall ²⁰	Individuals with anxiety and alcohol use disorders.	Various treatments for anxiety and alcohol use disorders.	Not specified.	Comorbidity and treatment considerations for anxiety and alcohol use disorders.

Gimeno <i>et al.</i> , ⁶ P, Balanzá- Martínez V, Alvarez FJ (2017)	Individuals with comorbid alcohol dependence and anxiety disorder.	Various treatments for comorbid alcohol depen- dence and anxiety disorder.	Not specified	Review of scientific evidence and recommen- dations for treatment of comorbid alcohol dependence and anxiety disorder.
Megan E. Castle, Meghan E. Flanigan (2024)	Individuals consuming excessive alcohol and experiencing withdrawal.	Examination of brain serotonin signaling.	Not specified	Call for more research in females regarding the role of brain serotonin signaling in excessive alcohol consumption and withdrawal.

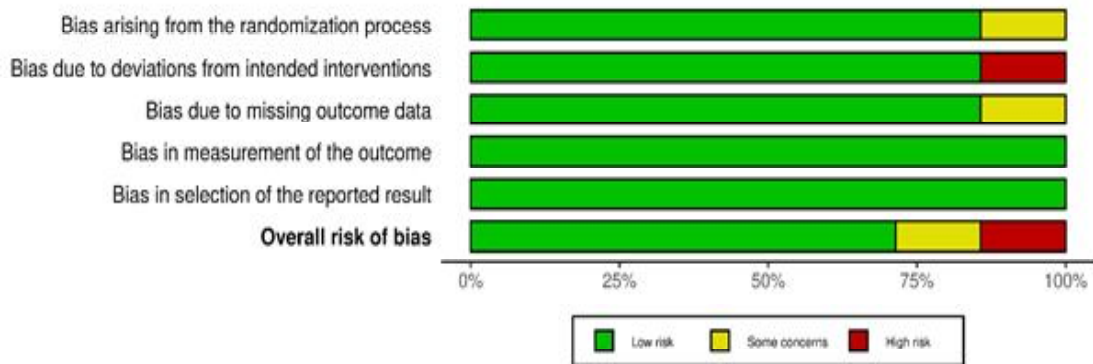


Figure 2. Risk of bias assessment;

Treating anxiety associated with alcohol use disorder (AUD) typically involves a combination of medication, psychotherapy, and lifestyle changes. Medications include selective serotonin reuptake inhibitors like sertraline and paroxetine. Alcohol affects neurotransmitters in the brain, such as gamma-aminobutyric acid (GABA) and glutamate. GABA is an inhibitory neurotransmitter that reduces brain activity, while glutamate is an

excitatory neurotransmitter that increases it. Alcohol initially increases GABA activity, leading to relaxation. Chronic alcohol use can lead to a decrease in GABA production and impair the functioning of GABA receptors⁶. This results in a state of GABA deficiency, where the brain becomes less responsive to the calming effects of GABA. Serotonin also plays a significant role in the anxiety induced by alcohol usage. Alcohol consumption

disrupts the balance of serotonin in the brain. Initially, alcohol can increase serotonin levels, leading to feelings of euphoria and relaxation. However, chronic alcohol use can deplete serotonin levels, leading to increased anxiety and depression. Alcohol affects the way serotonin receptor's function. Both short-term and long-term alcohol use can alter the effectiveness of serotonin receptors, impacting the brain's ability to regulate mood and anxiety¹³. The interplay between alcohol, GABA, and anxiety can create a vicious cycle. Individuals may drink to self-medicate their anxiety, but this only exacerbates the problem in the long run.

Chavyadi Churna is an Ayurvedic formulation which has been specifically indicated in *Madatyaya* or *Panatyaya*. It is interesting to note that the formulation is to be administered in the patient along with *Madya*. Intake of excess *Madya* causes *Annarasa Sankleda* and *Vidagha* due to its *Amla Rasa Pradhana Dravya* with *Tikshna, Ushna* and *Vidahi Guna*. Due to these inherent properties of *Madya*, when taken in excess it transforms into a substance with *Kshara Guna* which leads to the manifestation of *Antardaha, Jwara, Trushna, Pramoha, Vibhrama* and *Mada* instantaneously. To combat the above-mentioned symptoms *Madya* has been specified as a *Sahapana*, in this formulation because the *Amla Rasa* of *Madya* interacts with the *Kshara* present in the body of the patient, thereby leading to the production of *Madhura Rasa*¹⁷. Modern management of AUD doesn't contain medications which help in anxiety induced by AUD and treats the addiction to alcohol. Disulfiram, commonly

known as Antabuse, is primarily used in the treatment of chronic alcoholism. Its mode of action in this context is not directly associated with anxiety relief, but rather with the management of alcohol dependency. Disulfiram inhibits the enzyme aldehyde dehydrogenase, which is responsible for metabolizing acetaldehyde, a toxic byproduct of alcohol metabolism. When alcohol is consumed while on disulfiram, acetaldehyde accumulates in the body, leading to unpleasant symptoms such as flushing, palpitations, nausea, and vomiting. This aversive reaction reduces the desire to consume alcohol. The negative physiological effects triggered by disulfiram following alcohol intake can create a conditioned aversion to alcohol, contributing to abstinence in individuals with a history of chronic alcoholism¹⁹. Some studies suggest that discontinuing alcohol consumption in chronic drinkers may improve overall mental health and reduce anxiety symptoms over time, particularly if alcohol use was a coping mechanism for anxiety⁸. Thus, while disulfiram itself does not have an anxiolytic effect, its role in promoting sobriety can lead to better management of anxiety in the long run. However, the relationship between alcohol cessation and mental health can result in improved outcomes for individuals struggling with both issues. The specific mode of administration of *Chavyadi Churna* i.e., along with alcohol might implicate possibility of such a mechanism of action which culminates into effective alcohol withdrawal and AUD associated anxiety management.

The formulation has five basic ingredients which have almost similar *Rasapanchaka* as mentioned in Table-2.

Table-2. *Rasa Panchaka* of the ingredients of *Chavyadi Churna*

Name of the drug	<i>Chavya</i> ¹⁶	<i>Hingu</i> ¹⁷	<i>Mathulunga</i> ³	<i>Mahoushada</i> ⁴	<i>Ajamoda</i> ⁴
B.N	<i>Piper chaba</i>	<i>Ferula asafoetida</i>	<i>Citrus medica</i>	<i>Zingiber officianale</i>	<i>Apium graveolens</i>
<i>Rasa</i>	<i>Katu</i>	<i>Katu</i>	<i>Amla, Madhura</i>	<i>Katu</i>	<i>Katu, Tikta</i>
<i>Guna</i>	<i>Laghu, Ruksha</i>	<i>Laghu, Snigdha</i>	<i>Laghu, Snigdha</i>	<i>Guru, Ruksha</i>	<i>Laghu, Ruksha</i>
<i>Virya</i>	<i>Ushna</i>	<i>Ushna</i>	<i>Ushna</i>	<i>Ushna</i>	<i>Ushna</i>
<i>Vipaka</i>	<i>Katu</i>	<i>Katu</i>	<i>Amla</i>	<i>Madhura</i>	<i>Katu</i>
<i>Karma</i>	<i>Kaphahara, Vatahara, Deepana, Pachana</i>	<i>Kaphahara, Vatahara, Shoolahara, Bedhaniya, Anulomana</i>	<i>Vatahara, Kaphahara, Deepana, Hrudy</i>	<i>Vatahara, Kaphahara, Deepana, Bhedana</i>	<i>Kaphahara, Vatahara, Deepana, Hrudy Balya</i>

Chavyadi Churna has been indicated in *Vataja Panatyaya*. Ayurveda is a holistic system of medicine. Thus, maintaining the normal homeostasis of the body along with deaddiction is the core aim of *Madatyaya/Panatyaya Chikitsa*. Since *Madya* affects the *Rasavaha, Raktavaha* and *Samjavaha Srotas*, alcohol dependency shows symptoms such as *Ojokshaya* and *Dhatukshaya*. *Ojovardhaka, Dhathuvar dhaka* and *Balavardhaka Dravya* should be resorted to combat this pathophysiology. Symptoms such as *Sharirakampa, Bhrama, Pralapa* and *Anidra* indicate neurological manifestation of alcohol which can be compared with the descending order of CNS depression from cortex to medulla and further effect of GABA receptor by alcohol. *Medhya Dravya* and *Samjasthapana Dravya* has a major role in dealing with these neurological as well as psychological symptoms. The formulation has

predominance of *Katurasapradhana Dravya* with *Ushna Virya, Laghu Guna* and *Katu Vipaka*. Moreover, all the drugs are *Vatakaphahara* in *Doshaghnatha*. These properties of the ingredients help in *Srotovishodhana* of the *Srotas*, thus breaking down the pathophysiology. It has been observed that drugs with anxiolytic properties which stimulates the GABA receptors have been administered in other systems of medicine as well for alcohol deaddiction.

Chavyadi Churna has been formulated with drugs which have a combined effect of several activities. Instead of symptomatic treatment, each of the ingredient has a specific role in the condition. It has been observed that AUD and withdrawal has insomnia as one of the cardinal symptom. Piperine and Piperlonguminine, present in *Piper chaba* possess sedative properties which helps in reducing

agitation and promoting sleep. It has been postulated that these compounds increase the levels of neurotransmitters like dopamine and serotonin in the brain, which can help improve mood and cognitive function. Additionally, piperine has been shown to inhibit monoamine oxidase (MAO), an enzyme that breaks down neurotransmitters, potentially leading to a calming effect¹⁰. Myrcene present in *Citrus medica* also possess sedative effects and helps in reducing anxiety². Alkaloids such as Piperamine and pellitorine, flavonoids such as quercetin and naringenin and terpenoids such as β -caryophyllene and caryophyllene oxide present in *Piper chaba* are found to be responsible for its anxiolytic property⁷. In animal studies, the extract was administered orally and demonstrated significant anxiolytic effects, suggesting its potential use in managing anxiety. *Piper chaba*'s ethanolic extract has been shown to enhance the activity of GABA, a neurotransmitter that promotes relaxation and reduces anxiety. By increasing gabaergic activity, *Piper chaba* helps to calm the nervous system and alleviate anxiety symptoms. Asafoetida contains compounds that help neutralize free radicals in the body, reducing oxidative stress which is often linked to anxiety and other stress-related disorders. Volatile oils such as pinene, camphene, limonene, and fenchone, Resins like ferulic acid and umbelliferone and Organic disulfides unique to Asafoetida, contribute to the antioxidant activity of asafoetida⁵. Limonene, the primary component present in *Citrus medica* along with α -Pinene and β -caryophyllene have been shown to have calming effects on the nervous system². Zingerone, Gingerols, Shogaols and Paradols are also known for their anxiolytic properties and are present in *Zingiber*

*officinale*¹¹. Essential Oils present in *Apium graveolens* which include Phthalides particularly 3-n-butylphthalide (3nBP), Terpenes like limonene and pinene and Sesquiterpenes such as β -caryophyllene are potent anxiolytic agents¹⁸. Anti-inflammatory phytoconstituents present in all the individual herbal drugs stabilises the cell membranes, thereby reducing inflammation which help in reducing the physical discomfort associated with alcohol withdrawal. Thus, treating oxidative stress and inflammation helps us to combat anxiety associated with AUD effectively. This pharmacological potency of the formulation also aids in neuroprotective effect which is crucial in repairing and protecting brain cells damaged by chronic alcohol intake.

The treatment of anxiety associated with alcohol use disorder requires a multifaceted approach that includes both pharmacotherapy and psychotherapy. While SSRIs, buspirone, and gabapentin show promise, integrated treatment strategies that address both anxiety and alcohol use are crucial. Ayurvedic interventions, including herbal formulations, mind-body therapies, and yoga, show promise in alleviating anxiety and other withdrawal symptoms in individuals with alcohol use disorder. Clinical reports and case studies document improvements in both psychological and physical domains, supporting the potential of Ayurveda as a complementary approach in the management of AUD-related anxiety¹⁹. However, larger controlled studies are needed to further validate these findings and establish standardized protocols. *Chavyadi Churna* can be thus, a potent drug in the deaddiction regimen of Alcohol Use Disorder to effectively combat with anxiety associated with chronic

alcohol dependency as well as alcohol withdrawal. Looking at the current statistics of anxiety associated with alcohol dependency and withdrawal; complementary and integrative medicine can be probed further for therapeutically effective drug candidates with less adverse effects and holistic management. Pre-clinical evaluation and clinical data generating evidence-based data on the potency of *Chavyadi Churna* and many such formulations can bring forth further scope for treatment and research in the field. Future research should focus on rigorous trials on this novel therapeutic agent to improve outcomes for this complex comorbidity.

Registration and protocol

Since the review is not limited to only experimental animal studies and human trials, it was not registered in PROSPERO. Protocol was prepared but has not been published.

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There are no competing interests and no conflict of interest among review authors.

Author contributions

NJ: Conceptualization, Data collection, Writing original draft

LCS: Data interpretation, Writing original draft, review and editing

SB: Review, editing, Supervision

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