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MEDICATIONS FOR ALCOHOLISM AND MEASURES TO IMPROVE THEM

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ABOUT ARTICLE

Key words: Alcoholism, drugs, therapy, alcohol dependence syndrome, pharmacological treatments, psychosocial therapies, improve treatment availability.

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Abstract: Despite alcohol misuse being a significant sociological and economic issue for hundreds of years, no single effective treatment has been discovered. The intricacy of the pathophysiology of alcohol dependence makes it appear impossible to locate a single medication as a cure-all. This narrative review's goal is to examine current and perhaps upcoming medications for the most economical treatment of alcoholism. The FDA has approved acamprosate, disulfiram, and naltrexone, while the EMA has approved nalmefene. These medications are available to supplement psychotherapy, which is the cornerstone of treatment for alcoholism. The possibility of treating alcoholism with baclofen, topiramate, varenicline, and gabapentin has been reported recently in the literature. Furthermore, the outcomes of recent clinical trials utilizing psychoactive drugs like MDMA and psilocybin seem to represent a breakthrough in the current treatment of alcoholism. Despite this early hope, much more research is required before new pharmacological treatments for alcohol dependency syndrome are broadly accessible. In conclusion, combining pharmaceutical therapy with psychosocial therapies is the most successful approach to managing AUD. The available drugs for treating AUD have demonstrated good overall efficacy, despite the limitations of this review's narrative form.

However, more advancements can be made by combining different drugs and tailoring the treatment to each patient. The gap between patients who require treatment and those who receive it can be closed by improving practitioners' understanding of these drugs. Crucially, these drugs may also contribute to the development of precision medicine and individualized care for the diverse AUD population. Nonetheless, there is still a huge need to de-stigmatize and encourage treatment-seeking for AUD, expand the menu of approved pharmaceutical therapies, and improve treatment availability.

ALKOGOLIZMNI DAVOLASH UCHUN DORI VOSITALARI VA ULARNI TAKOMILLASHTIRISH CHORALARI

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MAQOLA HAQIDA

Kalit so‘zlar: alkogolizm, dori vositalari, terapiya, alkogolga qaramlik sindromi, farmakologik davolash, psixososial terapiyalar, davolash imkoniyatlarini yaxshilash.

Annotatsiya: Spirtli ichimliklarni suiiste’mol qilish yuzlab yillar davomida muhim ijtimoiy va iqtisodiy muammo bo‘lib kelganiga qaramay, uni davolashning yagona samarali usuli hanuzgacha topilmagan. Alkogolga qaramlik patofiziologiyasining murakkabligi uni to‘liq davolaydigan yagona dori vositasini topishni deyarli imkonsiz qilib ko‘rsatadi. Ushbu narrativ sharhning maqsadi alkogolizmni eng tejamkor davolash uchun hozirda mavjud va ehtimol kelajakda qo‘llanilishi mumkin bo‘lgan dori vositalarini ko‘rib chiqishdan iborat. FDA tomonidan akamprosat, disulfiram va naltrekson tasdiqlangan, Yevropa Dori vositalari agentligi (EMA) esa nalmefeneni tasdiqlagan. Ushbu dori vositalari alkogolizmni davolashning asosiy usuli hisoblangan psixoterapiyani qo‘llab-quvvatlash uchun ishlatiladi. So‘nggi yillarda adabiyotlarda baklofen, topiramat, vareniklin va gabapentin yordamida alkogolizmni davolash imkoniyati haqida xabarlar berilmoqda. Bundan tashqari, MDMA va psilotsibin kabi psixoaktiv moddalar qo‘llanilgan so‘nggi klinik

tadqiqotlar natijalari alkogolizmni davolashda muhim yutuq bo‘lishi mumkinligini ko‘rsatmoqda. Ushbu dastlabki umidlarga qaramay, alkogolga qaramlik sindromini davolash uchun yangi farmakologik usullar keng miqyosda qo‘llanilishidan oldin yana ko‘plab tadqiqotlar talab etiladi. Xulosa qilib aytganda, dori vositalari bilan davolashni psixososial terapiyalar bilan birlashtirish AUD (alkogol iste’moli buzilishi)ni boshqarishning eng samarali yondashuvidir. Ushbu sharhning narrativ shakliga xos cheklovlarga qaramay, AUDni davolash uchun mavjud dori vositalari umumiy samaradorlikni ko‘rsatgan. Biroq, turli dori vositalarini birlashtirish va davolashni har bir bemorga moslashtirish orqali yanada katta yutuqlarga erishish mumkin. Shifokorlarning ushbu dori vositalari haqidagi bilimlarini oshirish davolanishga muhtoj bo‘lgan bemorlar va uni olayotgan bemorlar o‘rtasidagi tafovutni kamaytirishga yordam beradi. Eng muhimi, ushbu dori vositalari turli AUD populyatsiyasi uchun aniqlik tibbiyoti va individuallashtirilgan parvarish rivojiga hissa qo‘shishi mumkin. Shunga qaramay, AUDni stigmatizatsiyadan xoli qilish va davolanishga murojaat qilishni rag‘batlantirish, tasdiqlangan farmatsevtik terapiyalar ro‘yxatini kengaytirish hamda davolash imkoniyatlarini yaxshilashga hali ham katta ehtiyoj mavjud.

ЛЕКАРСТВЕННЫЕ СРЕДСТВА ДЛЯ ЛЕЧЕНИЯ АЛКОГОЛИЗМА И МЕРЫ ПО ИХ СОВЕРШЕНСТВОВАНИЮ

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О СТАТЬЕ

Ключевые слова: алкоголизм, лекарственные средства, терапия, синдром алкогольной зависимости, фармакологическое лечение, психосоциальная терапия, улучшение доступности лечения.

Аннотация: Несмотря на то, что злоупотребление алкоголем на протяжении сотен лет является значимой социальной и экономической проблемой, единого эффективного метода лечения до настоящего времени не найдено.

Сложность патофизиологии алкогольной зависимости делает практически невозможным поиск универсального лекарственного средства. Цель данного нарративного обзора — рассмотреть современные и потенциально перспективные лекарственные препараты для наиболее экономически эффективного лечения алкоголизма. Управлением по контролю за продуктами и лекарствами США (FDA) одобрены акампросат, дисульфирам и налтрексон, а Европейским агентством по лекарственным средствам (EMA) — налмефен. Эти препараты применяются в дополнение к психотерапии, которая является основой лечения алкоголизма. В последние годы в литературе сообщается о возможности лечения алкоголизма с использованием баклофена, топирамата, варениклина и габапентина. Кроме того, результаты недавних клинических исследований с применением психоактивных веществ, таких как МДМА и псилоцибин, могут представлять собой прорыв в современном лечении алкоголизма. Несмотря на эти первоначальные обнадеживающие данные, перед широким внедрением новых фармакологических методов лечения синдрома алкогольной зависимости необходимы дополнительные исследования. В заключение следует отметить, что сочетание фармакотерапии с психосоциальными методами является наиболее эффективным подходом к лечению AUD (расстройства, связанного с употреблением алкоголя). Несмотря на ограничения нарративного характера данного обзора, доступные лекарственные средства для лечения AUD продемонстрировали хорошую общую эффективность. Однако дальнейший прогресс возможен за счет комбинирования различных препаратов и индивидуализации лечения для каждого пациента. Повышение осведомленности специалистов о данных лекарственных средствах поможет сократить разрыв между пациентами, нуждающимися в лечении, и теми, кто его получает. Важно отметить, что эти препараты также могут способствовать развитию прецизионной медицины и

индивидуализированного подхода к лечению различных групп пациентов с AUD. Тем не менее, по-прежнему существует значительная потребность в снижении стигматизации AUD, поощрении обращения за лечением, расширении перечня одобренных фармакологических методов терапии и улучшении доступности лечения.

Introduction. Numerous drugs have been explored over the past few decades to treat alcohol use disorder (AUD). Disulfiram, acamprosate, naltrexone, nalmefene, sodium oxybate, and baclofen are among those that have been approved in various nations with varying specific indications. The American Psychiatric Association recommends topiramate as a therapeutic alternative for patients who do not tolerate or respond to approved medications, even though it is not approved for the treatment of AUD. The WHO reports that alcohol use disorder (AUD) causes three million fatalities each year. About 6% of Americans suffer from alcohol misuse; 1 in 12 males and 1 in 25 women have this health issue. A strong desire or sense of compulsion to drink alcohol, difficulty controlling substance use, withdrawal symptoms when substance use is cut back or stopped, neglect of other alternative pleasures, and continued substance use despite obvious negative consequences are all diagnostic criteria for alcohol use disorder (AUD). Alcohol misuse has numerous negative effects on one's health, social life, and economy. The average global economic cost of alcohol consumption is roughly 2.6% of GDP, according to a meta-analysis that included 29 studies [1-4]. Two-thirds of the expenses associated with alcohol use are indirect, such as lost productivity from absenteeism and early death, and one-third are direct, such as health care, alcohol-related crime, and drunk driving accidents. A low weekly alcohol intake of 0.1–7 drinks may protect the cardiovascular system, according to certain studies, but these findings are based on epidemiological research. Alcohol use, however, can cause oxidative stress, apoptosis, mitochondrial malfunction, and structural harm to the heart and circulatory system. It has been repeatedly shown that alcohol of any kind and its intermittent use can cause gout attacks. Alcohol misuse raises the risk of suicide attempts, dementia, cancer, heart disease, and auto accidents, according to a WHO report. According to a comprehensive study, drinking alcohol and having a hangover both affect short-term memory deficits, sustained attention, and psychomotor performance. Even though alcohol has been used and consumed for centuries, there is still no one-size-fits-all method for treating addiction [5-10]. Alcoholics Anonymous group therapy, which emphasize the 12-step program and non-pharmacological interventions, are the primary methods; drugs that help lessen alcohol cravings and the addict's desire for alcohol are still underprescribed. Peer-delivered recovery support services appear to be a somewhat successful intervention that

merits more study among other non-pharmacological strategies for influencing people with alcohol addiction. The present treatments for addicts are designed to encourage complete abstinence, but more lately, restricted drinking—also known as a harm-reduction strategy—seems to be a more appealing choice. The US Food and Drug Administration (FDA) has only approved acamprosate, disulfiram, and naltrexone as treatments for alcohol dependency syndrome thus far. Along with the three previously listed medicines, nalmefene is also approved for treatment by the European Medicines Agency (EMA) [11-16]. Reports on the use of baclofen and the encouraging outcomes of adding topiramate, varenicline, and gabapentin to treatment have surfaced recently. It appears challenging to put into practice the idea that a single medication, taken consistently and acting on a single bodily mechanism, could be successful in curing a patient's long-standing alcohol issue because of the heterogeneity of the alcohol dependence syndrome. Animal models have been used in research on several aspects of alcohol consumption, including alcohol-related organ damage, alcohol tolerance, and physical dependence on alcohol. Among other techniques, operant conditioning was employed in the research, and efforts were made to pinpoint the genes that influence an individual's propensity for alcoholism. Additionally, animal models were utilized to investigate the efficacy of medications used to treat AUD. In order to boost utilization and enhance care, it is imperative that new, varied, and efficient pharmacological treatment options for AUD be developed. The current review's main goal is to provide a clinical overview of AUD pharmacotherapies. In particular, this study identifies new and repurposed medicines "on the horizon" for which evidence suggests a potentially successful application toward the treatment of AUD and gives a brief summary of presently licensed medications [17-22].

The main purpose of the presented manuscript is a brief analysis of anti-alcohol drugs and measures to improve them based on the results of reputable scientific research.

Pharmacological AUD Treatments. The effectiveness, mode of action, and tolerability of approved, repurposed, and innovative pharmacotherapies for the treatment of AUD are covered in this qualitative literature review. As of 2018, the American Psychological Association (APA) recommends acamprosate and naltrexone for the treatment of alcohol use disorder (AUD), gabapentin and topiramate for individuals seeking to reduce alcohol use or achieve abstinence, and disulfiram for obtaining and maintaining sobriety exclusively. Pharmacotherapies for AUD that have been authorized or are in development are examined in the following sections. Information was acquired using qualitative PubMed literature searches, and medications were chosen for this qualitative review based on the expertise of the authors and gaps in previous review publications. Based on the status of pharmacological approval, this evaluation is divided into three sections: (a) authorized pharmaceuticals, (b) repurposed (i.e., off-label) medications, and (c) new compounds. The basic mechanism of action, preclinical research evaluating the medication's effectiveness in

reducing alcohol-related behaviors in animal models, and, when available, clinical results from human laboratory studies and randomized controlled trials (RCTs) are all examined within each medication section [7-11]. One of the most important priorities for AUD research has been determined to be medication development. Even though this profession has advanced significantly, there are still a number of issues that need to be addressed in order to fully reap the benefits of AUD medication. First, even though AUD is common, very few people seek treatment for it. The treatment gap must be closed before anyone can profit from the advancements in drug research discussed here. This will necessitate involvement at several levels, including public education regarding AUD and its therapies as well as prevention. By using proper terminology to characterize AUD and other substance use disorders and the individuals who are impacted by them, researchers and clinicians can contribute to these efforts by lessening the stigma associated with these conditions (table 1).

Table 1: Approved and developing pharmaceutical treatments for AUD.

Agents	Disulfiram	Acamprosate	Naltrexone	Ondansetron	Mifepristone
Mechanism of action	Dopamine beta-hydroxylase inhibitor and aldehyde dehydrogenase inhibitor	affects the action of glutamate	Opioid receptor antagonist	5-HT3 receptor antagonist	Glucocorticoid receptor antagonist
Approval status	FDA- and EMA-approved for AUD	FDA- and EMA-approved for AUD	FDA- and EMA-approved for AUD	Repurposed	Repurposed
Preclinical results	Results are mixed: long-term alcohol use causes disulfiram tolerance; severe drinking is prevented but not moderate consumption.	Place choice, withdrawal symptoms, and decreased ethanol consumption	Decreased sedation, motor impairment, ethanol predilection, and binge drinking	decreased voluntary ethanol consumption and blocked sensitization to locomotor stimulant effects	
Clinical results	Results were mixed; drinking outcomes improved when administered under supervision.	Results were mixed: longer cumulative abstinence period, lower likelihood of recurrence. Negative research reveals no advantages	Modest impact sizes; decreased likelihood of relapse, binge drinking, and cravings	Patients with early-onset AUD had fewer drinks per day and more days without alcohol.	

		above a placebo.			
Target outcome	Attain and sustain abstinence	Attain and sustain abstinence	Reduce alcohol consumption and attain and sustain sobriety	Reduce alcohol consumption and attain and sustain sobriety	

5-HT3 serotonin receptor 3, 5-HT2A serotonin receptor 2A, AUD alcohol use disorder, FDA US Food and Drug Administration, EMA European Medicines Agency, GABA gamma-aminobutyric acid, mGluR5 metabotropic glutamate receptor 5, PDE phosphodiesterase, and MIF macrophage migration inhibitory factor

Additionally, we look at each drug's tolerability and possible customized uses by identifying demographics where the medication would be especially beneficial and indicating treatment goals (drinking reduction, attainment, or maintenance of abstinence). The authors wrap off by outlining potential paths for the advancement of precision medicine and pharmaceutical therapies for AUD [20-23].

Innovative Agents. Novel agents that have not yet been authorized for usage are covered in the following sections. Since most of these drugs are still in the early stages of development, there are currently no clinical results on their use in treating AUD. ABT-436 is a highly specific oral vasopressin type 1B (V1B) receptor antagonist. V1B antagonists have been demonstrated to have positive effects in rat models of alcohol dependence, including reducing alcohol intake by alcohol-preferring and alcohol-dependent rats and attenuating reinstatement of alcohol self-administration. They also reduce basal hypothalamic-pituitary-adrenal (HPA) axis activity. The discovery that ABT-436 decreased smoking and alcohol consumption suggests that V1B antagonists may be used to treat alcohol and nicotine co-use. Diarrhea is the most frequent adverse effect of ABT-436, which is generally well tolerated in humans. Additionally, the findings suggest that drugs that target the vasopressin receptor may be especially beneficial for individuals who experience high amounts of stress [9-15]. A GHB analogue called N-[(4-Trifluoromethyl) benzyl] 4-methoxybutyramide (GET73) has demonstrated encouraging preclinical outcomes in vitro and in vivo as a possible treatment for AUD. GET73's neuroprotective potential as a AUD treatment

was demonstrated when it was added to cultured of rat hippocampus neurons, which prevented adverse ethanol-induced effects, decreased cell viability, and increased reactive oxygen species generation. In vivo, GET73 therapy at low, non-sedative dosages (5–50 mg/kg) had anxiolytic effects, decreased alcohol consumption, and prevented relapse in alcohol-preferring rats. Although GET73 was shown to not attach to either high-affinity or low-affinity GHB binding sites in rat cortical membranes, these effects are comparable to those observed with GHB treatment. GET73 may function as a negative allosteric modulator at the metabotropic glutamate subtype 5 receptor (mGluR5), according to recent research, although its exact mode of action is yet unknown. Neither 30 nor 100 mg/kg GET73 given to rats (similar to levels used in humans) increased alcohol-induced drunkenness, according to a translational study looking at GET73-alcohol interactions. Furthermore, GET73 was well tolerated in two groups of 14 and 11 persons were given both with and without alcohol, with no significant adverse events and no variation in adverse events [16-22].

Potential Treatments in the Future. The primary hallucinogenic ingredient in some of the world's mushroom species is psilocybin. People who choose to consume psilocybin experience altered consciousness, greater introspection, hypnagogic experiences, and perceptual changes like synesthesia, delusions, and changes in the sense of time because of its agonism at the 5HT2a receptors. Due to its low toxicity, few adverse effects, and lack of addiction, psilocybin is regarded as a safe drug. As a result, its application is being studied all over the world, particularly in the management of depression. Psilocybin may help individuals with substance use problems improve their behavior, according to some authors. The recent 2022 randomized clinical experiment that showed psilocybin psychotherapy significantly reduces heavy drinking days in individuals with alcohol issues, surpassing active placebos and psychotherapy, lends credence to these hypotheses. It should be kept in mind that, despite the encouraging outcomes, there aren't many reports of this kind, and the idea is still in the experimental stage [5-12]. 3,4-Methylenedioxymethamphetamine, also known as MDMA or ecstasy, is a phenylethylamine that, about 60 minutes after oral consumption, releases a significant amount of serotonin into synaptic clefts, resulting in heightened sensations to audiovisual stimuli, increased empathy, and a sense of unity with the world. This substance has a variety of effects, including an abrupt rise in serotonin, direct action on α2-adrenergic, serotonin, histamine, β-adrenergic, and dopamine D1 and D2 receptors, and changes in prolactin, oxytocin, cortisol, adrenocorticotropic hormone, and vasopressin levels. Recent phase III clinical trials have validated MDMA's excellent efficacy and safety in treating post-traumatic stress disorder. Ben Sessa suggested in 2017 that MDMA-assisted psychotherapy (MDMA-AT) could be helpful in treating alcohol use disorders because it can improve the psychotherapeutic process and treat psychological trauma. MDMA-AT may potentially result in a subclinical improvement in alcohol consumption in patients with severe PTSD without raising

the risk of using illegal drugs, according to preliminary clinical observations from 2022. The development of MDMA-AT as an integrated treatment for PTSD, alcohol comorbidity, and substance use disorders is thus supported by preliminary data. It is encouraging to conduct more research in this area [17-22].

Discussion. Numerous drugs have been investigated for the treatment of alcohol use disorder (AUD) in recent decades. Disulfiram, acamprosate, naltrexone, nalmefene, sodium oxybate, and baclofen are among those that have been approved in various nations for various specific indications. The American Psychiatric Association recommends topiramate as a therapy option for patients who do not tolerate or respond to approved medications, even though it is not approved for the treatment of AUD. In this narrative review, we have examined the primary research that has been published in the literature, examining the safety and effectiveness of these drugs and determining whether or not they were focused on abstinence. Our research focused on randomized controlled studies that examined larger populations over longer time periods. This narrative review aims to discuss the effectiveness of these drugs in lowering alcohol intake and cravings, achieving complete alcohol abstinence, and preventing relapse in AUD patients. Additionally reported are their primary indications for treating AUD as both abstinence-oriented and non-abstinence-oriented drugs [3-9]. Keywords included alcohol use disorder, pharmaceutical treatment, acamprosate, baclofen, disulfiram, nalmefene, naltrexone, and topiramate. All studies published between the 1950s and the present were included in the literature search, with a primary focus on those published during the last ten years that had larger study samples, longer durations, and randomized-controlled designs. The results of AUD treatment vary greatly between persons and drugs. Only 16% of patients receiving treatment for AUD achieve abstinence, despite the fact that it may be desirable. Additionally, there is insufficient evidence to recommend abstinence as the sole strategy for treating AUD. Only 2–6% of goals in patient-driven therapy are focused on achieving alcohol abstinence, indicating that not all people with AUD view this as a goal of their recovery [11-17]. Recovering from non-abstinence, which includes cutting back on alcohol use in general and heavy drinking in particular (e.g., controlled drinking/harm reduction), has gained popularity as a therapeutic goal due to its acknowledged health and social benefits. It has been demonstrated that non-abstinent AUD recovery can last up to ten years after therapy. However, despite increasing awareness of the advantages of harm reduction, disulfiram—a drug expressly recommended for abstinence—remains the most often given pharmacotherapy for AUD. Furthermore, it is doubtful that a single drug will work for every person with a AUD due to the variability of AUD. In order to boost utilization and enhance care, it is imperative that new, varied, and efficient pharmacological treatment options for AUD be developed. The current review's main goal is to provide a clinical overview of AUD pharmacotherapies. In particular, this study

identifies new and repurposed medicines "on the horizon" for which evidence suggests a potentially successful application toward the treatment of AUD and gives a brief summary of presently licensed medications. Even if the drugs already on the market to treat AUD are very effective, individualized approaches can still lead to additional advancements. Furthermore, many patients lack access to specialized care, and these drugs are still noticeably underutilized in clinical practice [18-23].

Conclusions. The combination of pharmaceutical medication and psychosocial interventions is the most successful AUD management approach. The present drugs for the treatment of AUD have demonstrated good overall efficacy, despite the limitations of this review's narrative approach. However, more advancements can be made by combining different medications and tailoring the treatment to each patient. The gap between patients who require treatment and those who receive it can be closed by educating professionals about these drugs.

In summary, the three commonly prescribed drugs for AUD—disulfiram, acamprosate, and naltrexone—are underutilized and only somewhat effective. The fact that no single drug is likely to work for every person with AUD is another problem brought on by the heterogeneity of AUD. As a result, it is essential to provide new, varied, and more effective pharmacotherapy choices as well as to increase treatment accessibility. The innovative and repurposed drugs discussed in this article show promise for treating AUD in the future. Furthermore, the aforementioned future trends present opportunities for advancements in precision medicine and tailored care for the diverse AUD population.

References:

1. Stokłosa I, Więckiewicz G, Stokłosa M, Piegza M, Pudlo R, Gorczyca P. Medications for the Treatment of Alcohol Dependence-Current State of Knowledge and Future Perspectives from a Public Health Perspective. Int J Environ Res Public Health. 2023 Jan 19;20(3):1870. doi: 10.3390/ijerph20031870.

2. Poznyak, V. · Fleischmann, A. · Rekve, D. ...The World Health organization's Global Monitoring System on Alcohol and Health Alcohol Res. 2014; 35:244-249.

3. Burnette, E.M., Nieto, S.J., Grodin, E.N. et al. Novel Agents for the Pharmacological Treatment of Alcohol Use Disorder. Drugs 82, 251–274 (2022). https://doi.org/10.1007/s40265-021-01670-3

4. Maccioni P, Lorrai I, Contini A, Leite-Morris K, Colombo G. Microinjection of baclofen and CGP7930 into the ventral tegmental area suppresses alcohol self-administration in alcohol-preferring rats. Neuropharmacology. 2018;136(Pt A):146–58.

5. Colombo G, Gessa GL. Suppressing effect of baclofen on multiple alcohol-related behaviors in laboratory animals. Front Psychiatry. 2018;9:475.

6. Foo JC, Vengeliene V, Noori HR, Yamaguchi I, Morita K, Nakamura T, et al. drinking levels and profiles of alcohol addicted rats predict response to nalmefene. Front Pharmacol. 2019;10:471.

7. Montesinos J, Gil A, Guerri C. nalmefene prevents alcohol-induced neuroinflammation and alcohol drinking preference in adolescent female mice: role of TLR4. Alcohol Clin Exp Res. 2017;41(7):1257–70.

8. Jacobsen JHW, Buisman-Pijlman FT, Mustafa S, Rice KC, Hutchinson MR. Antagonising TLR4-TRIF signalling before or after a low-dose alcohol binge during adolescence prevents alcohol drinking but not seeking behaviour in adulthood. Neuropharmacology. 2018;1(128):460–73.

9. Guillot A, Ren T, Jourdan T, Pawlosky RJ, Han E, Kim S-J, et al. Targeting liver aldehyde dehydrogenase-2 prevents heavy but not moderate alcohol drinking. Proc Natl Acad Sci USA. 2019;116(51):25974–81.

10. Castillo-Carniglia A, Keyes KM, Hasin DS, Cerdá M. Psychiatric comorbidities in alcohol use disorder. Lancet Psychiatry. 2019;6(12):1068–80. Witkiewitz K, Roos CR, Mann K, Kranzler HR. Advancing precision medicine for alcohol use disorder: replication and extension of reward drinking as a predictor of naltrexone response. Alcohol Clin Exp Res. 2019;43(11):2395–405.

11. Volkow ND, Gordon JA, Koob GF. Choosing appropriate language to reduce the stigma around mental illness and substance use disorders. Neuropsychopharmacology. 2021;46(13):2230–2.

12. Volkow ND, Gordon JA, Koob GF. Choosing appropriate language to reduce the stigma around mental illness and substance use disorders. Neuropsychopharmacology. 2021;46(13):2230–2.

13. Freeman TP, Hindocha C, Baio G, Shaban NDC, Thomas EM, Astbury D, et al. Cannabidiol for the treatment of cannabis use disorder: a phase 2a, double-blind, placebo-controlled, randomised, adaptive Bayesian trial. Lancet Psychiatry. 2020;7(10):865–74.

14. Walzer M, Marek GJ, Wu R, Nagata M, Han D. Single- and multiple-dose safety, tolerability, and pharmacokinetic profiles of ASP8062: results from 2 phase 1 studies. Clin Pharmacol Drug Dev. 2020;9(3):297–306.

15. Haass-Koffler CL, Perciballi R, Magill M, et al. An inpatient human laboratory study assessing the safety and tolerability, pharmacokinetics, and biobehavioral effect of GET 73 when co-administered with alcohol in individuals with alcohol use disorder. Psychopharmacology (Berl). 2022;239:35–46.

16. Campbell EJ, Norman A, Bonomo Y, Lawrence AJ. Suvorexant to treat alcohol use disorder and comorbid insomnia: plan for a phase II trial. Brain Res. 2020;1(1728):146597.

17. Back SE, Gray K, Ana ES, Jones JL, Jarnecke AM, Joseph JE, et al. N-Acetylcysteine for the treatment of comorbid alcohol use disorder and posttraumatic stress disorder: design and methodology of a randomized clinical trial. Contemp Clin Trials. 2020;91:105961.

18. Israel Y, Quintanilla ME, Ezquer F, Morales P, Santapau D, Berríos-Cárcamo P, Ezquer M, Olivares B, Herrera-Marschitz M. Aspirin and N-acetylcysteine co-administration markedly inhibit chronic ethanol intake and block relapse binge drinking: Role of neuroinflammation-oxidative stress self-perpetuation. Addict Biol. 2021;26(1):e12853.

19. Vanderkam P, Solinas M, Ingrand I, Doux N, Ebrahimighavam S, Jaafari N, et al. Effectiveness of drugs acting on adrenergic receptors in the treatment for tobacco or alcohol use disorders: systematic review and meta-analysis. Addiction. 2021;116(5):1011–20.

20. Sinha R, Wemm S, Fogelman N, Milivojevic V, Morgan PM, Angarita GA, et al. Moderation of Prazosin's efficacy by alcohol withdrawal symptoms. American Journal of Psychiatry [Internet]. 2020 [cited 2021 Sep 16]. https://doi.org/10.1176/appi.ajp.2020.20050609.

21. Burnette EM, Ray LA, Irwin MR, Grodin EN. Ibudilast attenuates alcohol cue-elicited frontostriatal functional connectivity in alcohol use disorder. Alcohol Clin Exp Res. 2021;45(10):2017–28.

22. Wallhed Finn S, Lundin A, Sjöqvist H, Danielsson A-K. Pharmacotherapy for alcohol use disorders—unequal provision across sociodemographic factors and co-morbid conditions. A cohort study of the total population in Sweden. Drug Alcohol Depend. 2021;227:108964.

23. Han B, Jones CM, Einstein EB, Powell PA, Compton WM. Use of medications for alcohol use disorder in the US: results from the 2019 national survey on drug use and health. JAMA Psychiatry [Internet]. 2021 [cited 2021 Jun 16]. https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2781290.