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# Alcohol Causes Various Health Impacts

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**ABSTRACT:** Alcohol, sometimes referred to by the chemical name ethanol, is a depressant drug that is the active ingredient in drinks such as beer, wine, and distilled spirits (hard liquor).[11] It is one of the oldest and most commonly consumed recreational drugs, causing the characteristic effects of alcohol intoxication ("drunkenness").[12] Among other effects, alcohol produces happiness and euphoria, decreased anxiety, increased sociability, sedation, impairment of cognitive, memory, motor, and sensory function, and generalized depression of central nervous system (CNS) function. Ethanol is only one of several types of alcohol, but it is the only type of alcohol that is found in alcoholic beverages or commonly used for recreational purposes; other alcohols such as methanol and isopropyl alcohol are significantly more toxic.[11] A mild, brief exposure to isopropanol, being only moderately more toxic than ethanol, is unlikely to cause any serious harm. Methanol, being profoundly more toxic than ethanol, is lethal in quantities as small as 10–15 milliliters (2–3 teaspoons)

**KEYWORDS:** alcohol, beer, wine, intoxication, CNS, toxic, lethal, anxiety, sedation, hard liquor, euphoria, sensory

## I.INTRODUCTION

Alcohol has a variety of short-term and long-term adverse effects. Short-term adverse effects include generalized impairment of neurocognitive function, dizziness, nausea, vomiting, and hangover-like symptoms. Alcohol is addictive to humans, and can result in alcohol use disorder, dependence and withdrawal. It can have a variety of long-term adverse effects on health, such as liver and brain damage,[13][14][15] and its consumption can cause cancer.[16] The adverse effects of alcohol on health are most important when it is used in excessive quantities or with heavy frequency. However, some of them, such as increased risk of certain cancers, may occur even with light or moderate alcohol consumption.[17][18] In high amounts, alcohol may cause loss of consciousness or, in severe cases, death.

Alcohol works in the brain primarily by increasing the effects of γ-Aminobutyric acid (GABA),[19] the major inhibitory neurotransmitter in the brain; by facilitating GABA's actions, alcohol suppresses the activity of the CNS.[19] The substance also directly affects a number of other neurotransmitter systems including those of glutamate, glycine, acetylcholine, and serotonin.[20][21] The pleasurable effects of alcohol ingestion are the result of increased levels of dopamine and endogenous opioids in the reward pathways of the brain.[22][23] Alcohol also has toxic and unpleasant actions in the body, many of which are mediated by its byproduct acetaldehyde.[24]

Alcohol has been produced and consumed by humans for its psychoactive effects for almost 10,000 years.[25] Drinking alcohol is generally socially acceptable and is legal in most countries, unlike with many other recreational substances. However, there are often restrictions on alcohol sale and use, for instance a minimum age for drinking and laws against public drinking and drinking and driving.[26] Alcohol has considerable societal and cultural significance and has important social roles in much of the world. Drinking establishments, such as bars and nightclubs, revolve primarily around the sale and consumption of alcoholic beverages, and parties, festivals, and social gatherings commonly involve alcohol consumption. Alcohol is related to various societal problems, including drunk driving, accidental injuries, sexual assaults, domestic abuse, and violent crime.[27] Alcohol remains illegal for sale and consumption in a number of countries, mainly in the Middle East. While some religions, including Islam, prohibit alcohol consumption, other religions, such as Christianity and Shinto, utilize alcohol in sacrament and libation.[28][29][30]

Alcohol causes a plethora of detrimental effects in society.[27] Many emergency room visits involve alcohol use.[27] As many as 15% of employees show problematic alcohol-related behaviors in the workplace, such as drinking before going to work or even drinking on the job.[27] Drunk dialing refers to an intoxicated person making phone calls that they would not likely make if sober. Alcohol availability and consumption rates and alcohol rates are positively associated with nuisance, loitering, panhandling, and disorderly conduct in open spaces.[33]

Alcohol use is stereotypically associated with crime,[33] both violent and non-violent.[27] Some crimes are uniquely tied to alcohol, such as public intoxication or underage drinking, while others are simply more likely to occur together with alcohol consumption. Crime perpetrators are much more likely to be intoxicated than crime victims. Many alcohol laws have been passed to criminalize various alcohol-related activities.[33][34] Underage drinking and drunk driving are the most prevalent alcohol-specific offenses in the United States[33] and a major problem in many, if not most, countries

worldwide.[35][36][37] About one-third of arrests in the United States involve alcohol misuse,[27] and arrests for alcohol-related crimes constitute a high proportion of all arrests made by police in the U.S. and elsewhere.[38] In general, programs aimed at reducing society's consumption of alcohol, including education in schools, are seen as an effective long-term solution. Strategies aiming to reduce alcohol consumption among adult offenders have various estimates of effectiveness.[39] Policing alcohol-related street disorder and enforcing compliance checks of alcohol-dispensing businesses has proven successful in reducing public perception of and fear of criminal activities.[33]

In the early 2000s, the monetary cost of alcohol-related crime in the United States alone has been estimated at over $205 billion, twice the economic cost of all other drug-related crimes.[40] In a similar period in the United Kingdom, the cost of crime and its antisocial effects was estimated at £7.3 billion.[39] Another estimate for the UK for yearly cost of alcohol-related crime suggested double that estimate, at between £8 and 13 billion.[41] Risky patterns of drinking are particularly problematic in and around Russia, Mexico and some parts of Africa.[42] Alcohol is more commonly associated with both violent and non-violent crime than are drugs like marijuana.[27]

## II.DISCUSSION

The World Health Organization has noted that out of social problems created by the harmful use of alcohol, "crime and violence related to alcohol consumption" are likely the most significant issue.[42] In the United States, 15% of robberies, 63% of intimate partner violence incidents, 37% of sexual assaults, 45-46% of physical assaults and 40-45% of homicides (murders) involved use of alcohol.[43][40] A 1983 study for the United States found that 54% of violent crime perpetrators, arrested in that country, had been consuming alcohol before their offenses.[38] In 2002, it was estimated that 1 million violent crimes in the U.S. were related to alcohol use.[27] More than 43% of violent encounters with police involve alcohol.[27] Alcohol is implicated in more than two-thirds of cases of intimate partner violence.[27] Studies also suggest there may be links between alcohol abuse and child abuse.[33] In the United Kingdom, in 2015/2016, 39% of those involved in violent crimes were under alcohol influence.[44] International studies are similar, with an estimate that 63% of violent crimes worldwide involves the use of alcohol.[40]

The relation between alcohol and violence is not yet fully understood, as its impact on different individuals varies. Studies and theories of alcohol abuse suggest, among others, that use of alcohol likely reduces the offender's perception and awareness of consequences of their actions.[45][33][38][46] Heavy drinking is associated with vulnerability to injury, marital discord, and domestic violence.[27] Moderate drinkers are more frequently engaged in intimate violence than are light drinkers and abstainers, however generally it is heavy and/or binge drinkers who are involved in the most chronic and serious forms of aggression. Research found that factors that increase the likelihood of alcohol-related violence include difficult temperament, hyperactivity, hostile beliefs, history of family violence, poor school performance, delinquent peers, criminogenic beliefs about alcohol's effects, impulsivity, and antisocial personality disorder. The odds, frequency, and severity of physical attacks are all positively correlated with alcohol use. In turn, violence decreases after behavioral marital alcoholism treatment.[33]

A 2002 study found 41% of people fatally injured in traffic accidents were in alcohol-related crashes.[47] Misuse of alcohol is associated with more than 40% of deaths that occur in automobile accidents every year.[27] The risk of a fatal car accident increases exponentially with the level of alcohol in the driver's blood.[48]

Most countries have passed laws prohibiting driving a motor vehicle while impaired by alcohol. In the U.S., these crimes are generally referred to as Driving under the influence (DUI), although there are many naming variations among jurisdictions, such as driving while intoxicated (DWI).[49] With alcohol consumption, a drunk driver's level of intoxication is typically determined by a measurement of blood alcohol content or BAC; but this can also be expressed as a breath test measurement, often referred to as a BrAC. A BAC or BrAC measurement in excess of the specific threshold level, such as 0.08% in the U.S.,[50] defines the criminal offense with no need to prove impairment.[51] In some jurisdictions, there is an aggravated category of the offense at a higher BAC level, such as 0.12%, 0.15% or 0.25%. In many jurisdictions, police officers can conduct field tests of suspects to look for signs of intoxication.

Criminologist Hung-En Sung has concluded in 2016 that with regards to reducing drunk driving, law enforcement has not generally proven to be effective. Worldwide, the majority of those driving under the influence do not end up arrested. At least two thirds of alcohol-involved fatalities involve repeat drinking drivers. Sung, commenting on measures for controlling drunk driving and alcohol-related accidents, noted that the ones that have proven effective include "lowering legal blood alcohol concentrations, controlling liquor outlets, nighttime driving curfews for minors, educational treatment programs combined with license suspension for offenders, and court monitoring of high-risk offenders."[33]

Alcohol abuse increases the risk of individuals either experiencing or perpetrating sexual violence and risky, casual sex.[52] Caffeinated alcoholic drinks are particularly implicated.[53]

Often, a victim becomes incapacitated due to having consumed alcohol, which then facilitates sexual assault or rape, a crime known as drug-facilitated sexual assault.[54][55] Over 50% of reported rapes involve alcohol.[clarification needed][27] Alcohol remains the most commonly used predator drug,[56][57] and is said to be used in the majority of sexual assaults.[45] Many assailants use alcohol because their victims often willingly imbibe it, and can be encouraged to drink enough to lose inhibitions or consciousness. Sex with an unconscious victim is considered rape in most if not all jurisdictions, and some assailants have committed "rapes of convenience" whereby they have assaulted a victim after he or she had become unconscious from drinking too much.[58]

Public drunkenness or intoxication is a common problem in many jurisdictions. Public intoxication laws vary widely by jurisdiction, but include public nuisance laws, open-container laws, and prohibitions on drinking alcohol in public or certain areas. The offenders are often lower class individuals and this crime has a very high recidivism rate, with numerous instances of repeated instances of the arrest, jail, release without treatment cycle. The high number of arrests for public drunkenness often reflects rearrests of the same offenders.[38]

## III.RESULTS

Outbreaks of methanol poisoning have occurred when methanol is used to adulterate moonshine (bootleg liquor).[59] Methanol has a high toxicity in humans. If as little as 10 mL of pure methanol is ingested, for example, it can break down into formic acid, which can cause permanent blindness by destruction of the optic nerve, and 30 mL is potentially fatal,[60] although the median lethal dose is typically 100 mL (3.4 fl oz) (i.e. 1–2 mL/kg body weight of pure methanol[61]). Reference dose for methanol is 0.5 mg/kg/day.[62] Toxic effects take hours to start, and effective antidotes can often prevent permanent damage.[60] Because of its similarities in both appearance and odor to ethanol (the alcohol in beverages), it is difficult to differentiate between the two. Alcohol has a variety of short-term and long-term adverse effects. It also has reinforcement-related adverse effects, including addiction, dependence, and withdrawal. Alcohol use is directly related to considerable morbidity and mortality, for instance due to overdose and alcohol-related health problems.[63] Alcohol causes generalized CNS depression, is a positive allosteric $GABA_A$ modulator and is associated and related with cognitive, memory, motor, and sensory impairment. It slows and impairs cognition and reaction time and the cognitive skills, impairs judgement, interferes with motor function resulting in motor incoordination, loss of balance, confusion, sedation, numbness and slurred speech, impairs memory formation, and causes sensory impairment. At high concentrations, it can induce amnesia, analgesia, spins, stupor, and unconsciousness as result of high levels of ethanol in blood.

At very high concentrations, alcohol can cause anterograde amnesia, markedly decreased heart rate, pulmonary aspiration, positional alcohol nystagmus, respiratory depression, shock, coma and death can result due to profound suppression of CNS function alcohol overdose and can finish in consequent dysautonomia.

Alcohol can cause nausea and vomiting in sufficiently high amounts (varying by person).

Alcohol stimulates gastric juice production, even when food is not present, and as a result, its consumption stimulates acidic secretions normally intended to digest protein molecules. Consequently, the excess acidity may harm the inner lining of the stomach. The stomach lining is normally protected by a mucosal layer that prevents the stomach from, essentially, digesting itself. However, in patients who have a peptic ulcer disease (PUD), this mucosal layer is broken down. PUD is commonly associated with the bacteria Helicobacter pylori, which secretes a toxin that weakens the mucosal wall, allowing acid and protein enzymes to penetrate the weakened barrier. Because alcohol stimulates the stomach to secrete acid, a person with PUD should avoid drinking alcohol on an empty stomach. Drinking alcohol causes more acid release, which further damages the already-weakened stomach wall.[65] Complications of this disease could include a burning pain in the abdomen, bloating and in severe cases, the presence of dark black stools indicate internal bleeding.[66] A person who drinks alcohol regularly is strongly advised to reduce their intake to prevent PUD aggravation.[66]

Ingestion of alcohol can initiate systemic pro-inflammatory changes through two intestinal routes: (1) altering intestinal microbiota composition (dysbiosis), which increases lipopolysaccharide (LPS) release, and (2) degrading intestinal mucosal barrier integrity – thus allowing LPS to enter the circulatory system. The major portion of the blood supply to the liver is provided by the portal vein. Therefore, while the liver is continuously fed nutrients from the intestine, it is also exposed to any bacteria and/or bacterial derivatives that breach the intestinal mucosal barrier. Consequently, LPS levels increase in the portal vein, liver and systemic circulation after alcohol intake. Immune cells in the liver respond to LPS with the production of reactive oxygen species, leukotrienes, chemokines and cytokines. These factors promote tissue inflammation and contribute to organ pathology.[67]

Alcoholism or its medical diagnosis alcohol use disorder refers to alcohol addiction, alcohol dependence, dipsomania, and/or alcohol abuse. It is a major problem and many health problems as well as death can result from excessive alcohol

use.[27][63] Alcohol dependence is linked to a lifespan that is reduced by about 12 years relative to the average person.[27] In 2004, it was estimated that 4% of deaths worldwide were attributable to alcohol use.[63] Deaths from alcohol are split about evenly between acute causes (e.g., overdose, accidents) and chronic conditions.[63] The leading chronic alcohol-related condition associated with death is alcoholic liver disease.[63] Alcohol dependence is also associated with cognitive impairment and organic brain damage.[27] Some researchers have found that even one alcoholic drink a day increases an individual's risk of health problems by 0.4%.[74]

Two or more consecutive alcohol-free days a week have been recommended to improve health and break dependence.[75][76]

The principal mechanism of action for ethanol has proven elusive and remains not fully understood.[19][83] Identifying molecular targets for ethanol has proven unusually difficult, in large part due to its unique biochemical properties.[83] Specifically, ethanol is a very low molecular weight compound and is of exceptionally low potency in its actions, causing effects only at very high (millimolar mM) concentrations.[83][84] For these reasons, unlike with most drugs, it has not yet been possible to employ traditional biochemical techniques to directly assess the binding of ethanol to receptors or ion channels.[83][84] Instead, researchers have had to rely on functional studies to elucidate the actions of ethanol.[83] Moreover, although it has been established that ethanol modulates ion channels to mediate its effects,[21] ion channels are complex proteins, and their interactions and functions are complicated by diverse subunit compositions and regulation by conserved cellular signals (e.g. signaling lipids).[19][83]

Much progress has been made in understanding the pharmacodynamics of ethanol over the last few decades.[20][83] While no binding sites have been identified and established unambiguously for ethanol at present, it appears that it affects ion channels, in particular ligand-gated ion channels, to mediate its effects in the CNS.[19][20][21][83] Ethanol has specifically been found in functional assays to enhance or inhibit the activity of a variety of ion channels, including the $GABA_A$ receptor, the ionotropic glutamate AMPA, kainate, and NMDA receptors, the glycine receptor,[85] the nicotinic acetylcholine receptors,[86] the serotonin 5-$HT_3$ receptor, voltage-gated calcium channels, and BK channels, among others.[19][20][21][87][88] However, many of these actions have been found to occur only at very high concentrations that may not be pharmacologically significant at recreational doses of ethanol, and it is unclear how or to what extent each of the individual actions is involved in the effects of ethanol.[83] In any case, ethanol has long shown a similarity in its effects to positive allosteric modulators of the $GABA_A$ receptor like benzodiazepines, barbiturates, and various general anesthetics.[19][83] Indeed, ethanol has been found to enhance $GABA_A$ receptor-mediated currents in functional assays.[19][83] In accordance, it is theorized and widely believed that the primary mechanism of action is as a $GABA_A$ receptor positive allosteric modulator.[19][83] However, the diverse actions of ethanol on other ion channels may be and indeed likely are involved in its effects as well.[20][83]

In 2007, it was discovered that ethanol potentiates extrasynaptic δ subunit-containing $GABA_A$ receptors at behaviorally relevant (as low as 3 mM) concentrations.[19][83][89] This is in contrast to previous functional assays of ethanol on γ subunit-containing $GABA_A$ receptors, which it enhances only at far higher concentrations (> 100 mM) that are in excess of recreational concentrations (up to 50 mM).[19][83][90] Ro15-4513, a close analogue of the benzodiazepine antagonist flumazenil (Ro15-1788), has been found to bind to the same site as ethanol and to competitively displace it in a saturable manner.[83][89] In addition, Ro15-4513 blocked the enhancement of δ subunit-containing $GABA_A$ receptor currents by ethanol in vitro.[83] In accordance, the drug has been found to reverse many of the behavioral effects of low-to-moderate doses of ethanol in rodents, including its effects on anxiety, memory, motor behavior, and self-administration.[83][89] Taken together, these findings suggest a binding site for ethanol on subpopulations of the $GABA_A$ receptor with specific subunit compositions via which it interacts with and potentiates the receptor.[19][83][89][91]

A 2019 study showed the accumulation of an unnatural lipid phosphatidylethanol (PEth) competes with $PIP_2$ agonist sites on lipid-gated ion channels.[92] This presents a novel indirect mechanism and suggests that a metabolite, not the ethanol itself, can affect the primary targets of ethanol intoxication. Many of the primary targets of ethanol are known to bind $PIP_2$ including $GABA_A$ receptors,[93] but the role of PEth will need to be investigated for each of the primary targets.

## IV.CONCLUSIONS

The reinforcing effects of alcohol consumption are mediated by acetaldehyde generated by catalase and other oxidizing enzymes such as cytochrome P-4502E1 in the brain.[94] Although acetaldehyde has been associated with some of the adverse and toxic effects of ethanol, it appears to play a central role in the activation of the mesolimbic dopamine system.[95]

Ethanol's rewarding and reinforcing (i.e., addictive) properties are mediated through its effects on dopamine neurons in the mesolimbic reward pathway, which connects the ventral tegmental area to the nucleus accumbens (NAcc).[96][97] One of ethanol's primary effects is the allosteric inhibition of NMDA receptors and facilitation of $GABA_A$ receptors (e.g.,

enhanced $GABA_A$ receptor-mediated chloride flux through allosteric regulation of the receptor).[98] At high doses, ethanol inhibits most ligand-gated ion channels and voltage-gated ion channels in neurons as well.[98]

With acute alcohol consumption, dopamine is released in the synapses of the mesolimbic pathway, in turn heightening activation of postsynaptic $D_1$ receptors.[96][97] The activation of these receptors triggers postsynaptic internal signaling events through protein kinase A, which ultimately phosphorylate cAMP response element binding protein (CREB), inducing CREB-mediated changes in gene expression.[96][97]

With chronic alcohol intake, consumption of ethanol similarly induces CREB phosphorylation through the $D_1$ receptor pathway, but it also alters NMDA receptor function through phosphorylation mechanisms;[96][97] an adaptive downregulation of the $D_1$ receptor pathway and CREB function occurs as well.[96][97] Chronic consumption is also associated with an effect on CREB phosphorylation and function via postsynaptic NMDA receptor signaling cascades through a MAPK/ERK pathway and CAMK-mediated pathway.[97] These modifications to CREB function in the mesolimbic pathway induce expression (i.e., increase gene expression) of ΔFosB in the NAcc,[97] where ΔFosB is the "master control protein" that, when overexpressed in the NAcc, is necessary and sufficient for the development and maintenance of an addictive state (i.e., its overexpression in the nucleus accumbens produces and then directly modulates compulsive alcohol consumption).[97][99][100][101]

## REFERENCES

1. WHO Expert Committee on Problems Related to Alcohol Consumption : second report. Geneva, Switzerland: World Health Organization. 2007. p. 23. ISBN 9789241209441. Retrieved 3 March 2015. ...alcohol dependence (is) a substantial risk of regular heavy drinking...
2. ^ Vengeliene V, Bilbao A, Molander A, Spanagel R (May 2008). "Neuropharmacology of alcohol addiction". British Journal of Pharmacology. 154 (2): 299–315. doi:10.1038/bjp.2008.30. PMC 2442440. PMID 18311194. (Compulsive alcohol use) occurs only in a limited proportion of about 10–15% of alcohol users....
3. ^ Gilman JM, Ramchandani VA, Crouss T, Hommer DW (January 2012). "Subjective and neural responses to intravenous alcohol in young adults with light and heavy drinking patterns". Neuropsychopharmacology. 37 (2): 467–77. doi:10.1038/npp.2011.206. PMC 3242308. PMID 21956438.
4. ^ Principles of Addiction: Comprehensive Addictive Behaviors and Disorders. Academic Press. 17 May 2013. pp. 162–. ISBN 978-0-12-398361-9.
5. ^ Holford NH (November 1987). "Clinical pharmacokinetics of ethanol". Clinical Pharmacokinetics. 13 (5): 273–92. doi:10.2165/00003088-198713050-00001. PMID 3319346. S2CID 19723995.
6. ^ Pohorecky LA, Brick J (1988). "Pharmacology of ethanol". Pharmacology & Therapeutics. 36 (2–3): 335–427. doi:10.1016/0163-7258(88)90109-x. PMID 3279433.
7. ^ Becker CE (September 1970). "The clinical pharmacology of alcohol". California Medicine. 113 (3): 37–45. PMC 1501558. PMID 5457514.
8. ^ [i] Levine B (2003). Principles of Forensic Toxicology. Amer. Assoc. for Clinical Chemistry. pp. 161–. ISBN 978-1-890883-87-4.
9. ^ Iber FL (26 November 1990). Alcohol and Drug Abuse as Encountered in Office Practice. CRC Press. pp. 74–. ISBN 978-0-8493-0166-7.
10. ^ Haynes, William M., ed. (2011). CRC Handbook of Chemistry and Physics (92nd ed.). Boca Raton, FL: CRC Press. p. 3.246. ISBN 1-4398-5511-0.
11. ^ Collins SE, Kirouac M (2013). "Alcohol Consumption". Encyclopedia of Behavioral Medicine: 61–65. doi:10.1007/978-1-4419-1005-9_626. ISBN 978-1-4419-1004-2.
12. ^ "10th Special Report to the U.S. Congress on Alcohol and Health: Highlights from Current Research" (PDF). National Institute of Health. National Institute on Alcohol Abuse and Alcoholism. June 2000. p. 134. Retrieved 21 October 2014. The brain is a major target for the actions of alcohol, and heavy alcohol consumption has long been associated with brain damage. Studies clearly indicate that alcohol is neurotoxic, with direct effects on nerve cells. Chronic alcohol abusers are at additional risk for brain injury from related causes, such as poor nutrition, liver disease, and head trauma.
13. ^ Bruha R, Dvorak K, Petrtyl J (March 2012). "Alcoholic liver disease". World Journal of Hepatology. 4 (3): 81–90. doi:10.4254/wjh.v4.i3.81. PMC 3321494. PMID 22489260.
14. ^ Brust JC (April 2010). "Ethanol and cognition: indirect effects, neurotoxicity and neuroprotection: a review". International Journal of Environmental Research and Public Health. 7 (4): 1540–57. doi:10.3390/ijerph7041540. PMC 2872345. PMID 20617045.

15. ^ Venkataraman A, Kalk N, Sewell G, Ritchie CW, Lingford-Hughes A (March 2017). "Alcohol and Alzheimer's Disease-Does Alcohol Dependence Contribute to Beta-Amyloid Deposition, Neuroinflammation and Neurodegeneration in Alzheimer's Disease?". Alcohol and Alcoholism. 52 (2): 151–158. doi:10.1093/alcalc/agw092. hdl:10044/1/42603. PMID 27915236.
16. ^ de Menezes RF, Bergmann A, Thuler LC (2013). "Alcohol consumption and risk of cancer: a systematic literature review". Asian Pacific Journal of Cancer Prevention. 14 (9): 4965–72. doi:10.7314/apjcp.2013.14.9.4965. PMID 24175760.
17. ^ Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, Pelucchi C, Bellocco R, Negri E, Corrao G, Rehm J, Boffetta P, La Vecchia C (February 2013). "Light alcohol drinking and cancer: a meta-analysis". Annals of Oncology. 24 (2): 301–8. doi:10.1093/annonc/mds337. PMID 22910838.
18. ^ Yasinski, Emma, Even If You Don't Drink Daily, Alcohol Can Mess With Your Brain, Discover (magazine), January 12, 2021
19. ^ Lobo IA, Harris RA (July 2008). "GABA(A) receptors and alcohol". Pharmacology Biochemistry and Behavior. 90 (1): 90–4. doi:10.1016/j.pbb.2008.03.006. PMC 2574824. PMID 18423561.
20. ^ Narahashi T, Kuriyama K, Illes P, Wirkner K, Fischer W, Mühlberg K, Scheibler P, Allgaier C, Minami K, Lovinger D, Lallemand F, Ward RJ, DeWitte P, Itatsu T, Takei Y, Oide H, Hirose M, Wang XE, Watanabe S, Tateyama M, Ochi R, Sato N (May 2001). "Neuroreceptors and ion channels as targets of alcohol". Alcoholism: Clinical and Experimental Research. 25 (5 Suppl ISBRA): 182S–188S. doi:10.1097/00000374-200105051-00030. PMID 11391069.
21. ^ Olsen RW, Li GD, Wallner M, Trudell JR, Bertaccini EJ, Lindahl E, Miller KW, Alkana RL, Davies DL (March 2014). "Structural models of ligand-gated ion channels: sites of action for anesthetics and ethanol". Alcoholism: Clinical and Experimental Research. 38 (3): 595–603. doi:10.1111/acer.12283. PMC 3959612. PMID 24164436.
22. ^ Charlet K, Beck A, Heinz A (2013). "The dopamine system in mediating alcohol effects in humans". Current Topics in Behavioral Neurosciences. 13: 461–88. doi:10.1007/7854_2011_130. ISBN 978-3-642-28719-0. PMID 21533679.
23. ^ Méndez M, Morales-Mulia M (June 2008). "Role of mu and delta opioid receptors in alcohol drinking behaviour". Current Drug Abuse Reviews. 1 (2): 239–52. doi:10.2174/1874473710801020239. PMID 19630722.
24. ^ Burcham PC (19 November 2013). An Introduction to Toxicology. Springer Science & Business Media. pp. 42–. ISBN 978-1-4471-5553-9.
25. ^ McGovern PE, Zhang J, Tang J, Zhang Z, Hall GR, Moreau RA, Nuñez A, Butrym ED, Richards MP, Wang CS, Cheng G, Zhao Z, Wang C (December 2004). "Fermented beverages of pre- and proto-historic China". Proceedings of the National Academy of Sciences of the United States of America. 101 (51): 17593–8. Bibcode:2004PNAS..10117593M. doi:10.1073/pnas.0407921102. PMC 539767. PMID 15590771.
26. ^ Babor T, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, et al. (2010). Alcohol: No Ordinary Commodity: Research and Public Policy (2nd ed.). Oxford: Oxford University Press. ISBN 978-0-19-955114-9. OCLC 656362316.
27. ^ Butcher JN, Hooley JM, Mineka SM (25 June 2013). Abnormal Psychology. Pearson Education. p. 370. ISBN 978-0-205-97175-6.
28. ^ Ruthven M (1997). Islam : a very short introduction. New York. ISBN 978-0-19-154011-0. OCLC 43476241.
29. ^ "Eucharist | Definition, Symbols, Meaning, Significance, & Facts". Encyclopedia Britannica. Retrieved 3 August 2021.
30. ^ Bocking B (1997). A popular dictionary of Shintō (Rev. ed.). Richmond, Surrey [U.K.]: Curzon Press. ISBN 0-7007-1051-5. OCLC 264474222.
31. ^ Nutt DJ, King LA, Phillips LD (November 2010). "Drug harms in the UK: a multicriteria decision analysis". Lancet. 376 (9752): 1558–65. CiteSeerX 10.1.1.690.1283. doi:10.1016/S0140-6736(10)61462-6. PMID 21036393. S2CID 5667719.
32. ^ Nutt D, King LA, Saulsbury W, Blakemore C (March 2007). "Development of a rational scale to assess the harm of drugs of potential misuse". Lancet. 369 (9566): 1047–53. doi:10.1016/s0140-6736(07)60464-4. PMID 17382831. S2CID 5903121.
33. ^ Sunga HE (2016). "Alcohol and Crime". The Blackwell Encyclopedia of Sociology. American Cancer Society. pp. 1–2. doi:10.1002/9781405165518.wbeosa039.pub2. ISBN 9781405165518.
34. ^ Trevor B, Katy H (1 April 2005). Understanding Drugs, Alcohol And Crime. McGraw-Hill Education (UK). p. 6. ISBN 9780335212576.
35. ^ "Drunk Driving Statistics in the US and Across the World". Law Office of Douglas Herring. 13 November 2017. Archived from the original on 22 September 2019. Retrieved 22 September 2019.

36. ^ "Drunk Driving Increasing Concern Worldwide". Voice of America. Retrieved 22 September 2019.
37. ^ Sweedler BM, Stewart K (2009). Verster JC, Pandi-Perumal SR, Ramaekers JG, de Gier JJ (eds.). Worldwide trends in alcohol and drug impaired driving. Drugs, Driving and Traffic Safety. Birkhäuser Basel. pp. 23–41. doi:10.1007/978-3-7643-9923-8_2. ISBN 9783764399238.
38. ^ Clinard M, Meier R (14 February 2007). Sociology of Deviant Behavior. Cengage Learning. p. 273. ISBN 9780495093350.
39. ^ McMurran M (3 October 2012). Alcohol-Related Violence: Prevention and Treatment. John Wiley & Sons. pp. 337–338. ISBN 9781118411063.
40. ^ McMurran M (3 October 2012). Alcohol-Related Violence: Prevention and Treatment. John Wiley & Sons. p. 37. ISBN 9781118411063.
41. ^ "WHO | Governments confront drunken violence". WHO. Archived from the original on 4 May 2014. Retrieved 22 September 2019.
42. ^ "Global status report on alcohol and health" (PDF). World Health Organization. 2011.
43. ^ "Alcohol-Related Crimes: Statistics and Facts". Alcohol Rehab Guide. Retrieved 3 September 2019.
44. ^ "Alcohol statistics". Alcohol Change UK. Retrieved 22 September 2019.
45. ^ Christopher P. Holstege; et al., eds. (25 October 2010). Criminal poisoning: clinical and forensic perspectives. Sudbury, Mass.: Jones and Bartlett Publishers. pp. 232. ISBN 978-0763744632.
46. ^ Dingwall G (23 July 2013). Alcohol and Crime. Routledge. pp. 160–161. ISBN 9781134029709.
47. ^ Hingson R, Winter M (2003). "Epidemiology and consequences of drinking and driving". Alcohol Research & Health. 27 (1): 63–78. PMC 6676697. PMID 15301401.
48. ^ Naranjo CA, Bremner KE (January 1993). "Behavioural correlates of alcohol intoxication". Addiction. 88 (1): 25–35. doi:10.1111/j.1360-0443.1993.tb02761.x. PMID 8448514.
49. ^ Driving Under the Influence: A Report to Congress on Alcohol Limits. U.S. Department of Transportation, National Highway Traffic Safety Administration. 1992. pp. 1–.
50. ^ "Legislative History of .08 per se Laws – NHTSA". NHTSA. National Highway Traffic Safety Administration. July 2001. Retrieved 21 July 2017.
51. ^ Nelson B. "Nevada's Driving Under the Influence (DUI) laws". NVPAC. Advisory Council for Prosecuting Attorneys. Archived from the original on 22 April 2017. Retrieved 3 July 2017.
52. ^ Chersich MF, Rees HV (January 2010). "Causal links between binge drinking patterns, unsafe sex and HIV in South Africa: its time to intervene". International Journal of STD & AIDS. 21 (1): 2–7. doi:10.1258/ijsa.2000.009432. PMID 20029060. S2CID 3100905.
53. ^ Ball NJ, Miller KE, Quigley BM, Eliseo-Arras RK (April 2021). "Alcohol Mixed With Energy Drinks and Sexually Related Causes of Conflict in the Barroom". Journal of Interpersonal Violence. 36 (7–8): 3353–3373. doi:10.1177/0886260518774298. PMID 29779427. S2CID 29150434.
54. ^ Hall JA, Moore CB (July 2008). "Drug facilitated sexual assault—a review". Journal of Forensic and Legal Medicine. 15 (5): 291–7. doi:10.1016/j.jflm.2007.12.005. PMID 18511003.
55. ^ Beynon CM, McVeigh C, McVeigh J, Leavey C, Bellis MA (July 2008). "The involvement of drugs and alcohol in drug-facilitated sexual assault: a systematic review of the evidence". Trauma, Violence & Abuse. 9 (3): 178–88. doi:10.1177/1524838008320221. PMID 18541699. S2CID 27520472.
56. ^ Alcohol Is Most Common 'Date Rape' Drug Archived 17 October 2007 at the Wayback Machine. Medicalnewstoday.com. Retrieved on 1 June 2011.
57. ^ Schwartz RH, Milteer R, LeBeau MA (June 2000). "Drug-facilitated sexual assault ('date rape')". Southern Medical Journal. 93 (6): 558–61. doi:10.1097/00007611-200093060-00002. PMID 10881768.
58. ^ Date Rape. Survive.org.uk (20 March 2000). Retrieved on 1 June 2011.
59. ^ "Application to Include Fomepizole on the WHO Model List of Essential Medicines" (PDF). November 2012. p. 10.
60. ^ Vale A (2007). "Methanol". Medicine. 35 (12): 633–4. doi:10.1016/j.mpmed.2007.09.014.
61. ^ "Methanol Poisoning Overview". Antizol. Archived from the original on 5 October 2011. Retrieved 11 October 2011. dead link
62. ^ Methanol (CASRN 67-56-1)
63. ^ Friedman HS (26 August 2011). The Oxford Handbook of Health Psychology. Oxford University Press, USA. pp. 699–. ISBN 978-0-19-534281-9.

64. ^ Hendler RA, Ramchandani VA, Gilman J, Hommer DW (2013). "Stimulant and sedative effects of alcohol". Current Topics in Behavioral Neurosciences. 13: 489–509. doi:10.1007/7854_2011_135. ISBN 978-3-642-28719-0. PMID 21560041.
65. ^ Overview of Peptic Ulcer Disease: Etiology and Pathophysiology. Medscape.com. Retrieved 27 April 2013.
66. ^ Peptic Ulcer Disease (Stomach Ulcers) Cause, Symptoms, Treatments. Webmd.com. Retrieved 27 April 2013.
67. ^ Patel S, Behara R, Swanson GR, Forsyth CB, Voigt RM, Keshavarzian A (October 2015). "Alcohol and the Intestine". Biomolecules. 5 (4): 2573–88. doi:10.3390/biom5042573. PMC 4693248. PMID 26501334.
68. ^ Adams KE, Rans TS (December 2013). "Adverse reactions to alcohol and alcoholic beverages". Annals of Allergy, Asthma & Immunology. 111 (6): 439–45. doi:10.1016/j.anai.2013.09.016. PMID 24267355.
69. ^ Yost DA (2002). "Acute care for alcohol intoxication" (PDF). Postgraduate Medicine Online. 112 (6). Archived from the original (PDF) on 14 December 2010. Retrieved 29 September 2007.
70. ^ Arts NJ, Walvoort SJ, Kessels RP (27 November 2017). "Korsakoff's syndrome: a critical review". Neuropsychiatric Disease and Treatment. 13: 2875–2890. doi:10.2147/NDT.S130078. PMC 5708199. PMID 29225466.
71. ^ "More than 3 million US women at risk for alcohol-exposed pregnancy". Centers for Disease Control and Prevention. 2 February 2016. Retrieved 3 March 2016. 'drinking any alcohol at any stage of pregnancy can cause a range of disabilities for their child,' said Coleen Boyle, Ph.D., director of CDC's National Center on Birth Defects and Developmental Disabilities.
72. ^ Agents Classified by the IARC Monographs, Volumes 1–111 Archived 25 October 2011 at the Wayback Machine. monographs.iarc.fr
73. ^ "Triglycerides". American Heart Association. Archived from the original on 27 August 2007. Retrieved 4 September 2007.
74. ^ Bakalar N (27 August 2018). "How Much Alcohol Is Safe to Drink? None, Say These Researchers". The New York Times. Retrieved 17 September 2018.
75. ^ Tomlinson A (26 June 2018). "Tips and Tricks on How to Cut Down on the Booze". The West Australian. Seven West Media (WA). Retrieved 22 March 2019.
76. ^ "Alcohol". British Liver Trust. Archived from the original on 11 July 2019. Retrieved 22 March 2019.
77. ^ Laizure SC, Mandrell T, Gades NM, Parker RB (January 2003). "Cocaethylene metabolism and interaction with cocaine and ethanol: role of carboxylesterases". Drug Metabolism and Disposition. 31 (1): 16–20. doi:10.1124/dmd.31.1.16. PMID 12485948.
78. ^ Sakalo VS, Romanenko AM, Klimenko IA, Persidskiĭ I (1988). "Effects of chemotherapy on regional metastases of non-seminomatous tumors of the testis". Voprosy Onkologii. 34 (10): 1219–24. PMID 3188424.
79. ^ Lukas SE, Orozco S (October 2001). "Ethanol increases plasma Delta(9)-tetrahydrocannabinol (THC) levels and subjective effects after marihuana smoking in human volunteers". Drug and Alcohol Dependence. 64 (2): 143–9. doi:10.1016/S0376-8716(01)00118-1. PMID 11543984.
80. ^ Repchinsky C (ed.) (2012). Compendium of pharmaceuticals and specialties, Ottawa: Canadian Pharmacists Association.
81. ^ D'Souza S, Mayock S, Salt A (December 2017). "A review of in vivo and in vitro aspects of alcohol-induced dose dumping". AAPS Open. 3 (1). doi:10.1186/s41120-017-0014-9. ISSN 2364-9534.
82. ^ McCoy HG, Cipolle RJ, Ehlers SM, Sawchuk RJ, Zaske DE (November 1979). "Severe methanol poisoning. Application of a pharmacokinetic model for ethanol therapy and hemodialysis". The American Journal of Medicine. 67 (5): 804–7. doi:10.1016/0002-9343(79)90766-6. PMID 507092.
83. ^ Santhakumar V, Wallner M, Otis TS (May 2007). "Ethanol acts directly on extrasynaptic subtypes of GABAA receptors to increase tonic inhibition". Alcohol. 41 (3): 211–21. doi:10.1016/j.alcohol.2007.04.011. PMC 2040048. PMID 17591544.
84. ^ Spanagel R (April 2009). "Alcoholism: a systems approach from molecular physiology to addictive behavior". Physiological Reviews. 89 (2): 649–705. doi:10.1152/physrev.00013.2008. PMID 19342616.
85. ^ Söderpalm B, Lidö HH, Ericson M (November 2017). "The Glycine Receptor-A Functionally Important Primary Brain Target of Ethanol". Alcoholism: Clinical and Experimental Research. 41 (11): 1816–1830. doi:10.1111/acer.13483. PMID 28833225.
86. ^ Wu J, Gao M, Taylor DH (March 2014). "Neuronal nicotinic acetylcholine receptors are important targets for alcohol reward and dependence". Acta Pharmacologica Sinica. 35 (3): 311–5. doi:10.1038/aps.2013.181. PMC 4647894. PMID 24464050.

87. ^ Dopico AM, Bukiya AN, Kuntamallappanavar G, Liu J (2016). "Modulation of BK Channels by Ethanol". International Review of Neurobiology. 128: 239–79. doi:10.1016/bs.irn.2016.03.019. ISBN 978-0-12-803619-8. PMC 5257281. PMID 27238266.

88. ^ Möykkynen T, Korpi ER (July 2012). "Acute effects of ethanol on glutamate receptors". Basic & Clinical Pharmacology & Toxicology. 111 (1): 4–13. doi:10.1111/j.1742-7843.2012.00879.x. PMID 22429661.

89. ^ Wallner M, Olsen RW (May 2008). "Physiology and pharmacology of alcohol: the imidazobenzodiazepine alcohol antagonist site on subtypes of GABAA receptors as an opportunity for drug development?". British Journal of Pharmacology. 154 (2): 288–98. doi:10.1038/bjp.2008.32. PMC 2442438. PMID 18278063.

90. ^ Harrison NL, Skelly MJ, Grosserode EK, Lowes DC, Zeric T, Phister S, Salling MC (August 2017). "Effects of acute alcohol on excitability in the CNS". Neuropharmacology. 122: 36–45. doi:10.1016/j.neuropharm.2017.04.007. PMC 5657304. PMID 28479395.

91. ^ Förstera B, Castro PA, Moraga-Cid G, Aguayo LG (2016). "Potentiation of Gamma Aminobutyric Acid Receptors (GABAAR) by Ethanol: How Are Inhibitory Receptors Affected?". Frontiers in Cellular Neuroscience. 10: 114. doi:10.3389/fncel.2016.00114. PMC 4858537. PMID 27199667.

92. ^ Chung HW, Petersen EN, Cabanos C, Murphy KR, Pavel MA, Hansen AS, et al. (January 2019). "A Molecular Target for an Alcohol Chain-Length Cutoff". Journal of Molecular Biology. 431 (2): 196–209. doi:10.1016/j.jmb.2018.11.028. PMC 6360937. PMID 30529033.

93. ^ Laverty D, Desai R, Uchański T, Masiulis S, Stec WJ, Malinauskas T, et al. (January 2019). "Cryo-EM structure of the human α1β3γ2 $GABA_A$ receptor in a lipid bilayer". Nature. 565 (7740): 516–520. Bibcode:2019Natur.565..516L. doi:10.1038/s41586-018-0833-4. PMC 6364807. PMID 30602789.

94. ^ Karahanian E, Quintanilla ME, Tampier L, Rivera-Meza M, Bustamante D, Gonzalez-Lira V, Morales P, Herrera-Marschitz M, Israel Y (April 2011). "Ethanol as a prodrug: brain metabolism of ethanol mediates its reinforcing effects". Alcoholism: Clinical and Experimental Research. 35 (4): 606–12. doi:10.1111/j.1530-0277.2011.01439.x. PMC 3142559. PMID 21332529.

95. ^ Melis M, Enrico P, Peana AT, Diana M (November 2007). "Acetaldehyde mediates alcohol activation of the mesolimbic dopamine system". The European Journal of Neuroscience. 26 (10): 2824–33. doi:10.1111/j.1460-9568.2007.05887.x. PMID 18001279. S2CID 25110014.

96. ^ "Alcoholism – Homo sapiens (human) Database entry". KEGG Pathway. 29 October 2014. Retrieved 9 February 2015.

97. ^ Kanehisa Laboratories (29 October 2014). "Alcoholism – Homo sapiens (human)". KEGG Pathway. Retrieved 31 October 2014.

98. ^ Malenka RC, Nestler EJ, Hyman SE (2009). "Chapter 15: Reinforcement and Addictive Disorders". In Sydor A, Brown RY (eds.). Molecular Neuropharmacology: A Foundation for Clinical Neuroscience (2nd ed.). New York: McGraw-Hill Medical. p. 372. ISBN 978-0-07-148127-4.

99. ^ Ruffle JK (November 2014). "Molecular neurobiology of addiction: what's all the (Δ)FosB about?". The American Journal of Drug and Alcohol Abuse. 40 (6): 428–37. doi:10.3109/00952990.2014.933840. PMID 25083822. S2CID 19157711.

100. ^ Nestler EJ (December 2013). "Cellular basis of memory for addiction". Dialogues in Clinical Neuroscience. 15 (4): 431–43. doi:10.31887/DCNS.2013.15.4/enestler. PMC 3898681. PMID 24459410. Despite the Importance of Numerous Psychosocial Factors, at its Core, Drug Addiction Involves a Biological Process: the ability of repeated exposure to a drug of abuse to induce changes in a vulnerable brain that drive the compulsive seeking and taking of drugs, and loss of control over drug use, that define a state of addiction. ... A large body of literature has demonstrated that such ΔFosB induction in D1-type NAc neurons increases an animal's sensitivity to drug as well as natural rewards and promotes drug self-administration, presumably through a process of positive reinforcement

101. ^ Robison AJ, Nestler EJ (October 2011). "Transcriptional and epigenetic mechanisms of addiction". Nature Reviews. Neuroscience. 12 (11): 623–37. doi:10.1038/nrn3111. PMC 3272277. PMID 21989194.