Risk Management and Healthcare Policy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Alcohol in Daily Products: Health Risks, Cultural Considerations, and Economic Impacts

Yedi Herdiana

Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, 45363, Indonesia

Correspondence: Yedi Herdiana, Email y.herdiana@unpad.ac.id

Abstract: Ethanol, a bioactive compound prevalent in both social and industrial applications, is present in alcoholic beverages as well as a range of everyday products. In food, ethanol functions primarily as an additive or a by-product of fermentation, while in pharmaceuticals and cosmetics, it serves as a solvent or preservative. Despite its widespread use, three critical research gaps exist in current literature. First, existing research focuses predominantly on single-sector analyses, overlooking the cumulative effects of cross-sectoral ethanol exposure. Second, despite growing global market integration, there is limited understanding of how cultural and religious requirements influence ethanol-related regulations and product formulations. Third, current economic models fail to integrate both health impact costs and cultural compliance expenses, hindering effective policy development. The World Health Organization has determined that no amount of alcohol consumption can be considered entirely safe, as ethanol's health impacts include contributions to chronic diseases, neurotoxicity, and potential carcinogenic effects. These risks are compounded by the pervasive and often unrecognized presence of ethanol in various products, particularly affecting vulnerable populations. The economic burden associated with alcohol-related issues, including lost productivity and healthcare costs, highlights the necessity for robust public health strategies and stringent regulatory guidelines. This review investigates ethanol's role across multiple domains, emphasizing its presence in food, medicine, cosmetics, and industrial products, and evaluates its broader implications for public health, cultural practices, and economic impact. This review recommend implementing standardized labeling systems, establishing cultural-sensitive alternatives in product formulations, and developing harmonized international guidelines for ethanol use across industries.

Keywords: ethanol safety standards, public health risk management, acetaldehyde, stress oxidative, cultural-sensitive product

Introduction

Ethanol, widely recognized as alcohol, is a bioactive substance with a multifaceted role in modern society.[1] It is consumed as an alcoholic beverage and used extensively in various industrial applications, including pharmaceuticals, cosmetics, household products, solvents, and biofuels.[2] Ethanol is also present in numerous foods either as an intentional additive or a by-product of fermentation, such as in fruits, juices, breads, and sauces.[3,4] Despite its ubiquitous presence, the health implications of ethanol, particularly for vulnerable groups such as children, pregnant women, and individuals recovering from alcohol dependence, necessitate a thorough examination of its exposure and regulatory guidelines.[5–7] Alcohol consumption may be associated with an increased risk of preterm births, though an exact dose-response relationship has not been established.[8]

Ethanol can be derived from biomass fermentation, known as bioethanol, or it can be synthesized from ethylene, a petroleum-based by-product.[2,9,10] Its diverse applications range from enhancing flavor and preserving food to serving as a solvent in pharmaceuticals and cosmetics.[11–14] This widespread use demands comprehensive risk assessments and clear regulatory guidelines to safeguard public health.

Moderate alcohol intake was once considered heart-healthy and endorsed by the American Heart Association (AHA). However, conflicting evidence from alcohol use disorder studies and recent research indicated no cardiovascular benefit and potential harm. By 2023, the AHA updated its guidelines, indicating that even one drink per day might elevate the risk of cardiovascular disease.[15] Increasing alcohol consumption is associated with heightened risks of disease and mortality.[16,17]

Received: 19 September 2024
Accepted: 17 November 2024
Published: 18 January 2025

Identifying a safe level of alcohol consumption is critical but challenging. Recent studies suggest that the safest level of alcohol consumption is none, as even moderate drinking carries risks that often outweigh potential health benefits.[18,19] Exposure to ethanol from multiple sources poses significant health risks, particularly when accumulated in large amounts. However, the cumulative exposure to ethanol from these various sources complicates the assessment of its overall impact on health.[20–22] The study concludes that alcohol is a major global health issue, with even low levels of consumption heightening the risk of severe health issues, including cancer. This supports the UK Chief Medical Officer's guideline that there is no safe level of alcohol consumption.[18] The study suggests prioritizing public health policies that reduce alcohol consumption at the population level, such as increasing taxes, regulating prices, restricting marketing, and limiting availability. These measures are effective and cost-efficient, like those used for tobacco control. The UK is implementing these strategies, with Scotland already adopting minimum unit pricing (MUP) and similar measures planned for Northern Ireland and Wales.[18] The economic impact of ethanol use is substantial. In the United States alone, alcohol-related problems cost the economy an estimated $249 billion annually, primarily due to lost productivity, healthcare expenses, and enforcement costs. Similar economic burdens are observed globally, underscoring the necessity for comprehensive public health strategies, robust regulatory policies, and effective consumer education.[23–25]

Ethanol's presence in everyday products also raises cultural and religious issues. Under Islamic law, ethanol is generally considered non-halal (haram) if it acts as an intoxicant. However, ongoing debates focus on the acceptability of different types of ethanol in non-intoxicating products. Developing clear guidelines that respect religious beliefs while ensuring consumer safety is essential.[12,26]

A comprehensive risk assessment and well-defined regulatory guidelines regarding ethanol's presence in everyday products are crucial. Islamic teachings emphasize the protection of mental faculties, which has led to a gradual prohibition of alcohol, culminating in a complete ban. This review underscores the necessity for a stringent regulatory framework and public health strategies to mitigate ethanol's adverse effects while recognizing its industrial and social importance. It also examines how standards are implemented in countries with substantial Muslim populations to safeguard public health, respect cultural sensitivities, and manage economic costs effectively.

Overview of Alcohol

Ethanol, also called ethyl alcohol, is a primary alcohol derived from ethane by replacing one hydrogen atom with a hydroxyl group. Ethanol, also known as ethyl alcohol, is widely used in beverages, products, and medicines.[4,27,28] Typical alcoholic beverages include beer, wine, distilled spirits, as well as combinations of these or other additives like malt liquor, fortified wine, liqueur, and cordials.[29] In the food industry, ethanol's versatility makes it valuable as a solvent, preservative, and processing agent, and it is also a byproduct of fermentation in alcoholic beverages.[30] The FDA designates ethanol as a Generally Recognized as Safe (GRAS) substance for use in food products. However, ethanol must meet strict regulatory standards to ensure its safety for consumption. While moderate consumption is generally safe for most adults, excessive long-term use can lead to addiction and serious health issues.

Ethanol Production

Ethanol is a volatile compound produced through the fermentation of sugars. This process utilizes the enzyme zymase from yeast, which converts sugars into ethanol and carbon dioxide. Approximately 66% of global ethanol production is used for transportation, while 21% is allocated for industrial purposes.[31]

Ethanol is produced through the fermentation process, where yeast acts on carbohydrates in the absence of oxygen.[32] Most ethanol is generated by fermenting sucrose-rich crops, such as sugar cane and sugar beet, or starch-rich crops, like corn and other starchy grains, using the yeast Saccharomyces cerevisiae.[3] During fermentation, ethanol concentration increases up to about 15%. Beyond this level, the yeast becomes toxic, halting the fermentation process. Experimental data shows that ethanol content rises from 2.8969% after 144 hours to 3.7491% after 168 hours, demonstrating the impact of fermentation time on production.[33] Ethanol concentrations below 1% (w/v) are typically achieved through natural fermentation, where sugars are converted into ethanol, which is further transformed into acetic acid, carbon dioxide, and ethyl acetate. This process maintains an acidic environment ($pH \leq 4$) to prevent microbial spoilage, with ethanol levels between 0.2% and 1.0% ensuring effective preservation. When ethanol levels drop below 0.2%, acetic acid may over-oxidize, leading to an increase in pH above 4.7. Conversely, ethanol concentrations above 1% can cause the formation of ethyl acetate, which also raises the pH.[11]

In industrial settings, ethanol is produced not only through fermentation but also from various feedstocks such as ethylene, ethane, and glucose. While synthetic ethanol is chemically identical to fermented ethanol, achieving concentrations above 15% requires distillation. Ethanol and water form an azeotrope at 95.6%, so breaking this azeotrope and reaching higher concentrations involves using dehydrating agents or additives.[34]

There is growing interest in expanding the range of raw feedstocks for ethanol production to include lignocellulosic biomass and algae, in addition to traditional grain-based materials.[31] Effective production of bioethanol from lignocellulosic biomass relies on pretreatment processes that enhance biomass breakdown and improve ethanol yields. Techniques such as dilute acid and alkaline sodium sulfite treatments are crucial for this purpose. For example, pretreatment of corn stover resulted in 93.0% xylose recovery, 85.0% lignin removal, and a 48.5 g/L ethanol concentration.[35] However, bioethanol production faces challenges such as high enzyme costs and the presence of inhibitory compounds. Additionally, contamination by *Lactobacillus spp*. can produce organic acids that reduce fermentation efficiency.[36]

Advancements in bioconversion systems are essential for improving production efficiency and sustainability. Despite progress, achieving high saccharification rates and ethanol yields at an industrial scale remains a challenge. Future research aims to enhance enzyme performance, explore alternative feedstocks, and scale up production processes.[9] Research continues to focus on developing cost-effective enzymes, optimizing biomass structures, and addressing these issues.[37]

Ethanol is commercially produced via fermentation or chemical synthesis. During fermentation, ethanol is created along with carbon dioxide as a by-product from the breakdown of carbon sources like starch, sugar, or cellulose by yeast or bacteria. In contrast, synthetic ethanol is derived from ethylene, a by-product of petroleum refining. In the food and beverage industry, ethanol can be present either as a result of natural fermentation or as an added processing aid.[38] Bioethanol, produced from plant materials like corn stalks and wood chips, can be blended with gasoline to offer a cleaner, more resource-efficient fuel alternative to fossil fuels.[39] This renewable fuel supports sustainable energy goals and helps reduce greenhouse gas emissions.

Ethanol Types

Ethanol is utilized in various forms depending on its application, with distinct types serving specific functions across different industries: Pharmaceutical-Grade Ethanol, Food Grade Ethanol, Industrial Ethanol, Denatured Ethanol, Fuel Ethanol/ Bioethanol, Technical Grade Ethanol, and Hydrated Ethanol (Table 1).

Alcohol can be produced through biomass fermentation or synthesized by hydrating ethylene, either directly or indirectly. Various catalysts, such as silica gel, montmorillonite, and bentonite, are commonly used in the indirect hydration process, particularly in industrial settings.[47] However, producing synthetic ethanol can be expensive due to the significant energy required to compress ethylene and water when using phosphoric acid catalysts. In contrast, bioethanol production has become the preferred method for commercial ethanol because it is more cost-effective, relies on renewable resources like cereal grains, and avoids toxic chemicals found in petroleum-based alternatives. Many countries widely practice fermentation technology for producing fuel and potable ethanol, though the choice of feedstock varies by region.[10]

Ethanol and Health Disorders

When consumed, ethanol is swiftly absorbed from the stomach and small intestines into the bloodstream and then circulated to various tissues, including the brain. The rate of absorption can be influenced by factors such as body weight, food intake, and the speed of drinking. In the US, the legal blood-alcohol concentration (BAC) limit for driving is 0.08 g/dL. Alcohol absorption primarily occurs in the stomach and upper small intestine, with peak levels reached 30 to 60 minutes after consumption.[32] Once in the body, ethanol is mainly metabolized in the liver, where it is converted into acetaldehyde, a compound linked to hangover symptoms. Acetaldehyde is further broken down into acetic acid and then into CO_2 and H_2O. Additionally, a small portion of ethanol is also excreted through urine, breath, and sweat.[32] In small amounts, ethanol acts as a stimulant, but in larger quantities, it functions as a depressant, increasing the risk of various

Table 1 Various Type of Alcohol

No	Type	Description	Usage	Ref
1	Pharmaceutical-Grade Ethanol / Absolute Ethanol	Pharmaceutical alcohol (ethanol) is a highly purified alcohol that meets strict pharmacopoeia standards for use in medicines, disinfectants, and homeopathic products. The USP requires minimum purity standards with no more than 0.5% impurities by weight.	Pharmaceutical ethanol is highly purified alcohol used in medicines, disinfectants, and homeopathic products. Its purity prevents contamination and its low water content ensures efficient manufacturing processes.	[40–42]
2	Food-Grade Ethanol	Food-grade ethanol meets Food Chemicals Codex (FCC) purity standards, ensuring it's safe for human consumption.	FCC ethanol is used in food and beverage production for extracts, flavorings, and colorings, with strict safety regulations.	[40, 41]
3	Industrial Ethanol	Industrial ethanol follows American Society for Testing and Materials and Environmental Protection Agency standards, allowing up to 1% impurities - less pure than food and pharmaceutical grades. It's commonly used as a biofuel alternative to fossil fuels.	Industrial ethanol is used as a solvent in pharmaceuticals, cosmetics, cleaning products, paints, and varnishes due to its versatility and cost-effectiveness.	[42–44]
4	Fuel Ethanol/ Bioethanol	Ethanol serves as a renewable biofuel alternative to fossil fuels in transportation.	When blended with gasoline, ethanol can reduce carbon dioxide emissions by 90% and sulfur dioxide by 60–80%, helping decrease fossil fuel dependence.	[24, 25, 43]
5	Technical Grade Ethanol	Technical-grade ethanol may contain contaminants at much higher concentrations compared to USP or FCC compliant ethanol. It is typically used in industrial applications and is less refined.	May contain impurities acceptable for industrial use but not for consumption or medical use.	[40, 41]
6	Denatured Ethanol	Denatured ethanol typically has an alcoholic strength of 88–90% v/v. Ethanol intentionally made undrinkable by adding chemicals.	Used in cleaning products, disinfectants, and industrial solvents. Economically advantageous due to tax exemptions.	[42, 45]
7	Hydrated Ethanol	Ethanol with significant water content.	Hydrated ethanol is used in alcoholic beverages and some industrial processes. For biofuels, it can be used directly in engines, while anhydrous ethanol is blended with gasoline.	[46]

diseases. Alcohol consumption raises the risk of numerous health problems, as show in Table 2. It is a leading cause of death, particularly among young people and disadvantaged populations.[19]

Acetaldehyde, a carcinogenic compound, interferes with DNA synthesis and repair, leading to stable mutations such as N2-ethyl-deoxyguanosine. Approximately 40% of Asians have a deficiency in acetaldehyde dehydrogenase, resulting in higher acetaldehyde levels and a higher risk of cancers, especially in the upper gastrointestinal tract and colon. This highlights the critical role of acetaldehyde in alcohol-related cancer development, as it can cause damage independently of ethanol.[106–108] Additionally, ethanol metabolism generates oxidative stress, which contributes to various health issues, including cell damage, inflammation, liver disease, and cardiovascular problems. Reducing or avoiding alcohol is crucial to lowering the risk of cancer and other alcohol-related health disorders.[84]

Combining alcohol and tobacco greatly amplifies the risk of cancers in the oral cavity, pharynx, larynx, and esophagus, with the combined risk exceeding the sum of their individual risks. Alcohol is a Group 1 carcinogen associated with at least seven cancers, including bowel and breast cancer. Additionally, acetic acid, a metabolite of alcohol, can cause oxidative stress and alter arterial blood pressure.[15,106]

Table 2 Alcohol and Health Problems

No	Disease Category	Specific Disease or Condition	Mechanism	Ref
1	Liver Diseases	Alcoholic Liver Disease (ALD)	Chronic alcohol use triggers oxidative stress and gut leakage, disrupting bacteria and immunity. This leads to cirrhosis with symptoms like jaundice, bleeding, and confusion.	[8, 48]
		Cirrhosis	Excessive drinking causes liver scarring, leading to fatigue, bruising, jaundice, and potential liver failure.	[49, 50]
2	Cardiovascular Diseases	Hypertension	Heavy drinking increases blood pressure risk through insulin and stress hormones. Moderate drinking effects are less clear, with possible protective benefits.	[51–53]
		Cardiomyopathy	Alcohol toxicity can weaken heart muscle and enlarge ventricles through oxidative stress and metabolic disruption, impairing blood pumping function.	[54, 55]
		Arrhythmias	Alcohol interferes with the heart's electrical signals, causing irregular heartbeats, also known as arrhythmias.	[56, 57]
		Acute aortic dissection (AAD)	Alcohol damages blood vessels through oxidative stress and inflammation, activating harmful cellular pathways.	[58, 59]
3	Gastrointestinal Diseases	Gastritis	Alcohol inflames stomach lining, causing gastritis.	[60, 61]
		Pancreatitis	Alcohol inflames pancreas by activating digestive enzymes, causing tissue damage through toxic metabolites.	[52, 62]
		Gastroesophageal Reflux Disease (GERD)	Alcohol relaxes esophageal sphincter, causing acid reflux and heartburn.	[63–65]
		Alcohol-Associated Bowel Disease (ABD)	Alcohol's toxic byproducts damage intestinal barrier, causing inflammation and bacterial imbalance.	[66, 67]
4	Neurological Disorders	Wernicke-Korsakoff Syndrome	Alcohol depletes thiamine, damaging multiple brain regions.	[68, 69]
		Peripheral Neuropathy	Alcohol damages autonomic and sensory nerves, causing numbness and muscle weakness.	[70, 71]
		Dementia	Alcohol-related dementia (ARD) is a form of dementia resulting from prolonged heavy drinking, which causes neurological damage and cognitive impairment.	[72, 73]
5	Mental Health Disorders	Depression and Anxiety	Heavy drinking causes brain damage leading to cognitive decline (ARD).	[74, 75]
		Alcohol Use Disorder (AUD)	AUD is a condition characterized by the inability to control or stop alcohol consumption despite adverse effects on social, work, or health aspects of life. Individuals with AUD should be directed to mental health or addiction specialists for treatment, which may include counseling or medication	[76, 77]
6	Cancers	Oral and Throat Cancer	Alcohol Use Disorder (AUD) is uncontrolled drinking despite negative life impacts, requiring professional treatment.	[78]
		Esophageal Cancer	Alcohol's byproduct acetaldehyde increases esophageal cancer risk.	[79,80]
		Liver Cancer	Alcohol induces liver cancer through toxic byproducts, oxidative stress, immune dysfunction, and bacterial changes.	[81–83]

(*Continued*)

https://doi.org/10.2147/RMHP.S495493

Table 2 (Continued).

No	Disease Category	Specific Disease or Condition	Mechanism	Ref
		Breast Cancer	Body breaks down alcohol in two steps: first to toxic acetaldehyde, then to harmless acetic acid.	[84, 85]
		Colorectal Cancer	Alcohol enhances colorectal cancer growth by promoting cell survival and spread.	[86,87]
7	Immune System Suppression	Increased Susceptibility to Infections	Excessive drinking weakens immune system by reducing protective cells and antibodies.	[88,89]
8	Reproductive Health	Impotence and Infertility	Alcohol impairs male fertility by reducing sperm quality, hormones, and antioxidant levels.	[90–92]
9	Musculoskeletal Disorders	Osteoporosis	Alcohol weakens bones by disrupting bone cells and mineral-regulating hormones.	[93–96]
		Myopathy	Alcohol causes muscle weakness and breakdown (myopathy), in acute or chronic forms.	[97, 98]
		Bone repair and rebuilding	Alcohol slows bone healing but may not affect bone density.	[99]
10	Metabolic Disorders	Diabetes	Alcohol increases obesity and diabetes risk by disrupting blood sugar control.	[100, 101]
		Lipid Metabolism	Alcohol alters blood lipid profiles differently in men and women, affecting metabolic health.	[102]
11	Skin Conditions	Psoriasis and Dermatitis	Alcohol triggers and worsens psoriasis and other inflammatory skin conditions.	[103]
		Neoplastic skin diseases	Alcohol's metabolite interacts with UV rays, damaging DNA and increasing skin cancer risk.	[104]
12	Fetal development	Fetal alcohol spectrum disorders (FASD)	Alcohol during pregnancy causes lifelong physical and developmental impairments.	[5]
		Sepsis and respiratory infections in newborns	Alcohol depletes glutathione, increasing susceptibility to respiratory infections.	[7, 105]

Numerous studies highlight the necessity of large-scale randomized trials to conclusively ascertain the health impacts of alcohol consumption. This ongoing debate centres around the relationship between moderate alcohol intake and health risks, particularly its potential link to diabetes [106]. Clinicians should actively screen patients for alcohol use, especially those with an elevated risk of developing diabetes, and provide targeted counselling and resources. Establishing clear alcohol consumption guidelines is crucial in mitigating excessive intake. Many healthcare settings emphasize these guidelines, with specialties such as dermatology also advocating for reduced alcohol consumption, particularly in patients with conditions like psoriasis.[101,103]

Ethanol and Social Disorders

Alcoholism is a neurological disorder influenced by genetic factors, childhood trauma, social environment, mental illness, and notably early alcohol consumption, which significantly increases the risk of developing the condition.[23,109–111] In clinical forensic medicine, alcohol is associated with criminal behaviours such as traffic accidents, suicide, and sexual assault, as well as child abuse, partner violence, and parental abuse.[32]

Socially, alcohol use leads to disrupted family relationships, decreased work productivity, and increased criminal activity. Dependence often results in social isolation, with individuals prioritizing drinking over familial and social obligations. This contributes to higher absenteeism, workplace accidents, and increased healthcare costs. In conclusion, alcohol use disorder (AUD) significantly impacts families by adding burdens, disrupting social and financial stability, and causing psychological and health issues for both adults and children. Spouses often face increased emotional distress and health problems, while children may struggle with behavioural and academic difficulties. Addressing AUD effectively is crucial not only for the individual but also for the well-being of their entire family.

The NHS Digital Statistics Report indicates that approximately 900,000 hospital admissions annually are related to alcohol consumption. The NHS warns that alcohol intake during pregnancy can cause foetal alcohol spectrum disorders. Early alcohol use heightens the risk of developing heavy drinking habits and alcohol dependence in adulthood, and is linked to negative outcomes such as academic failure and violent behaviour.[112]

Treatment for alcohol dependence typically combines psychotherapy and pharmacotherapy, including detoxification and ongoing support such as group therapy. Medications like acamprosate, disulfiram, and naltrexone are commonly used. Despite advancements, relapse remains a challenge, underscoring the need for a comprehensive approach addressing psychological, social, and biological aspects of alcoholism.[109,113] Recent studies reveal that nanozyme agar treatment in rats with alcohol poisoning decreased blood alcohol levels by 55.8% after 300 minutes, while not increasing acetaldehyde levels.[114]

The concurrent use of cocaine and alcohol is a dangerous combination. Cocaine increases extracellular monoamines by inhibiting dopamine (DA), norepinephrine (NE), and serotonin (5-HT) transporters (DAT, NET, and SERT). Ethanol also raises extracellular monoamines but does so through different mechanisms. Research suggests that organic cation transporter 3 (OCT3) plays a crucial role in regulating monoamine signalling in this context.[115]

Ethanol Contents of Daily Consumption

Ethanol in Food and Drug Industry

The versatility of ethanol is proven in various applications, ranging from food processing and preservation to the use of fuel and antiseptics. Its various functions emphasize the importance of this product in various industries and everyday life (Table 3), while regulatory measures ensure the safe use of consumer products.

Table 3 Application of Ethanol in Food and Drug Industry

No	Application of Ethanol	Usage	Mechanism	Potential Residue	Ref
1	Solvent	Ethanol extracts essential oils, flavors, and fragrances from plants.	Ethanol's dual polarity dissolves both water-soluble and fat-soluble compounds.	Solvent Residues	[27, 37]
2	Preservative	Ethanol extends food shelf life by preventing microbial growth.	Ethanol preserves food by disrupting microbe membranes and proteins.	Ethanol Residues	[56, 116]
3	Food Processing	Ethanol used in decaffeination, oil extraction, and glycerin production.	Ethanol's solvent properties efficiently extract molecules from plant materials through dissolving and separation.	Ethanol and By-products	[57, 61]
4	Antiseptic	Ethanol is used as an antiseptic to disinfect skin and surfaces.	Ethanol kills microbes by disrupting cell membranes and proteins, effective at 60–70% concentration.	Ethanol Residues on Skin or Surfaces	[2, 106, 117]
5	Fuel	Ethanol blends with gasoline as renewable fuel source.	Ethanol burns cleaner than gasoline by producing fewer toxic byproducts and carbon emissions.	Ethanol Residues in By-products	[31, 101, 108]

 https://doi.org/10.2147/RMHP.S495493

Industrial food products for babies and children are regulated in various countries, particularly within the EU, to limit exposure to potentially toxic chemicals. Regulations cover additives, materials in contact with food, contaminants, and hygiene standards. Data on ethanol effects in children are limited, mostly focusing on acute poisoning or research in adults and animals. Ethanol can cause acute poisoning in children at 0.3 g/kg and can be fatal at 3 g/kg. There is insufficient data on low-dose ethanol effects in children. Both the French Medicines Agency and the FDA advise against using ethanol in children's medicines unless absolutely necessary, while the WHO recommends keeping ethanol levels below 0.5% in products for children under 6 years[118] Figure 1.[119]

Regulatory agencies like the FDA and EPA set stringent standards for residue levels to ensure the safety of food, pharmaceuticals, and other products. These standards are crucial in managing the risks associated with residual ethanol, ensuring that it remains within safe limits. To achieve this, manufacturing processes include various controls such as evaporation, purification, and rigorous quality checks. These measures help minimize the presence of residual ethanol and by-products in final products, maintaining high safety and quality standards. Consequently, while residual ethanol is a consideration, it is effectively managed through these regulatory and manufacturing practices to ensure it remains within acceptable and safe levels across different applications. Commercial products may contain ethanol added as a preservative, potentially at levels that disqualify them from halal certification.[38]

Alcohol Residues in Food and Drug

Ethanol is a key ingredient in various alcoholic beverages (beer, wine, spirits), fruit juices, salads, candies, burger rolls, sweet milk rolls, and fermented foods like yogurt and bread.[2] Several methods for determining ethanol content in processed foods and beverages focus on liquid matrices such as soy sauce, olive oil, and alcoholic drinks. Techniques include headspace extraction with gas chromatography-flame ionization detection (GC-FID) or gas chromatography-mass spectrometry (GC-MS), and a non-GC approach using microwave dielectric analysis. A validated method combines liquid-liquid extraction with dimethyl sulfoxide (DMSO) and GC-MS to detect ethanol in kimchi, soy sauce, and

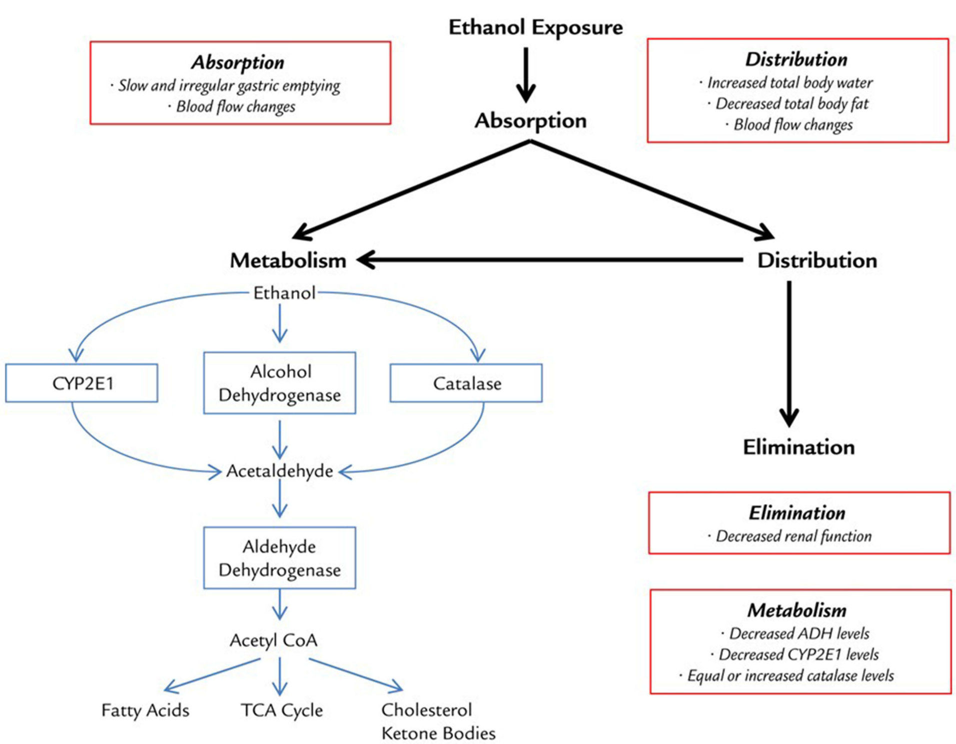

Figure 1 Ethanol disposition. Physiologic factors in neonates having the potential to affect the absorption, distribution, metabolism, and excretion of ethanol when compared with adults. Red boxes show infant-specific differences compared with adult. Reproduced with permission from Marek E, Kraft WK. Ethanol Pharmacokinetics in Neonates and Infants. Curr Ther Res. 2014;76:90–97. Open Access (http://creativecommons.org/licenses/by-nc-sa/3.0/).[119]

gochujang. Mansur et al proposed an aqueous extraction method with magnetic stirring for analyzing ethanol in complex matrices, offering a greener alternative to DMSO-based methods. Further research is needed to assess its reliability across different food and beverage matrices.[120]

Ethanol in Beverages

The terms "alcohol" and "alcoholic beverage" are often confused, though they refer to different concepts. Alcoholic beverages fall into three main categories: beer, wine, and spirits, with alcohol content ranging from 3% to 50%. Beer typically has 2–6% alcohol, wine about 10–12%, and spirits over 20%.[121] They are produced either by fermentation (eg, beer, wine, cider) or distillation (eg, whiskey, gin, vodka). Fermentation involves converting sugars in raw materials like grapes, grains, and fruits into ethanol, carbon dioxide, and energy through yeast action.[122] Alcoholic beverages are complex mixtures of ethanol, water, sugars, organic acids, proteins, phenolics, and volatile compounds, which define their sensory characteristics. Industrially produced alcoholic beverages include beers, wines, and various distilled spirits like brandy, whiskey, and tequila. Each beverage contains major components such as ethanol and water, and minor or trace elements like fusel alcohols, organic acids, and esters. Over 1300 compounds have been identified in different alcoholic beverages.[123,124]

Ethanol also increases the solubility of primary flavors in beer, which can aid processes such as dealcoholizing. In addition, processing Aglianico grapes with ethanol can significantly increase sugar, acid, and anthocyanin levels, thus improving the quality and composition of the grapes, especially in less than ideal conditions.[125]

Co-inoculation of *Hanseniaspora uvarum* with *Saccharomyces cerevisiae* reduces ethanol production and improves grape aroma quality, producing fruitier and ester aromas. Low ethanol grapes have a more prominent fruit flavor. Although promising, further research is needed for large-scale applications.[126]

Research findings show that the millennial generation's alcohol consumption behavior is influenced by functional, social, and emotional factors, with a tendency to spontaneously or planned alcohol consumption. The presence of methanol content in alcoholic beverages circulating in the market is a problem that the Government must pay attention to, and must warn the public that denatured alcohol contains methanol and is not safe for consumption.[45]

Ethanol in Food

Ethanol is commonly used as a food additive in various forms, serving as a solvent for flavorings and extracts, and enhancing the taste and aroma of food products. It also functions as a preservative in baked goods, extending their shelf life, and is involved in the production and as a carrier for certain food colorings. Ethanol is found in foods for several reasons, including the tolerable levels permitted in "non-alcoholic" beer and the presence of naturally occurring ethanol in bananas or fermented foods. Most food samples analyzed do not have ethanol concentrations high enough to present substantial risks from acute or chronic consumption by either adults or children.[127]

Although many food products contain low levels of ethanol, most do not pose a significant risk to adults or children, even with chronic consumption. For example, breads such as burger rolls and rye bread have alcohol levels between 1.18% and 1.28%, while yogurt and kefir range from 0.05% to 2%. Kombucha and must (usually made from grapes) contain 0.5% to 5% ethanol, and food additives, including extracts and flavorings, can have up to 35% alcohol content. Condiments like mustard and ketchup typically contain between 1.5% and 2% alcohol. Most critical are high chronic ethanol intakes when no labelling of ethanol exist (eg in fermented food).[127]

Although ethanol is present in various foods, risk assessments for low-dose exposure are limited. While small amounts generally pose minimal risk, even low doses may have toxicological implications. Chronic exposure data is insufficient to establish a safe dose, and most research focuses on higher ethanol levels from alcoholic beverages. Regulatory standards for ethanol in non-alcoholic beverages vary: in the US, drinks with ≤0.5% ethanol are considered non-alcoholic, while Canada and some Muslim-majority countries allow up to 1.1%, and the EU permits up to 1.2%. These differences reflect diverse cultural and legal views. Given the potential risks, even low ethanol levels should be minimized in foods to protect public health, as comprehensive studies on very low doses are lacking.[127]

Ethanol in Fruits

Ethanol levels in fresh fruits increase over time due to anaerobic sugar fermentation. For example, raw palm fruit initially has no ethanol, but levels rise to 0.6% in mature hanging fruit and 0.9%-4.5% in ripe fallen fruit. Similarly, fresh pineapple stored at 4°C for ten days saw its ethanol content increase from 0.48% to 1%. Fresh grape juice, on the other hand, had its ethanol concentration rise from 0.00029% to 2.11% after one day at room temperature, and reach 5.60% after ten days.[128]

Factors like low oxygen, high carbon dioxide, and storage temperature stress can increase ethanol production in fruits, causing unpleasant tastes. Key metabolic pathways involved include mitochondrial energy metabolism, glycolysis, and the Krebs cycle.[129] Higher temperatures accelerate ethanol evaporation and absorption, peaking at 20°C. Ethanol mainly converts to esters in apples and grapes, and to acetaldehyde in persimmons. It affects ethylene metabolism differently: reducing ethylene in apples at 20°C but increasing it in persimmons at 2°C, with little effect on respiration rates.[130]

Ethanol treatment delays ripening and preserves the storage quality of papaya. It extends the lifespan of cut Bougainvillea flowers, inhibits melon ripening, and prevents grapefruit rot. Additionally, ethanol slows broccoli yellowing and fruit senescence by eliminating bacteria, fungi, and viruses.[131]

The halal status of naturally fermented ethanol in food is debated. The GSO standard (2538:2017) sets the maximum residue level (MRL) of ethanol in fruit juice at 0.1% (v/v). Research found ethanol and sugar levels in stored fruit juice remained constant, supporting the GSO standard.[132] High ethanol levels in unfresh grape juice should be labeled non-Halal, so high-sugar fruits should be consumed fresh.[128]

Abundant fruit waste can be used to produce bioethanol due to its high sugar content.[133] Consistent exposure to ethanol-containing fruits may have influenced the evolution of metabolic enzymes in mammals.[134] Future research should explore more aspects of fruit ripening to understand its impact on fruit-eating animals.[135]

Long-term consumption of fruits and vegetables, particularly industrially processed ones, can lead to higher-than-expected alcohol exposure (mainly methanol and ethanol). This gradual exposure may contribute to cell and tissue damage and play a role in chronic diseases such as autism, liver diseases, cancer, diabetes, and neurological disorders, especially when combined with metabolic and genetic predispositions like folate deficiency and ADH variations.[118]

Ethanol in Drug

Ethanol is commonly used in oral pharmaceutical formulations as a cosolvent to enhance the solubility of poorly soluble drugs and as a preservative, with concentrations ranging from 0.6% to 76% v/v.[136] Despite guidelines from the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on acceptable ethanol levels, many medications contain higher amounts.[137]

Ethanol, used in pharmaceuticals and cosmetics, enhances the absorption of active ingredients into the skin.[138] For example, Phenobarbital Elixir BP is the sole licensed liquid phenobarbital formulation in the UK. Ethanol improves the flexibility of ethosomes for deep skin penetration and is employed in transdermal drug delivery systems, enhancing skin permeability when combined with water.[139,140] It is also used in creating antibacterial and antioxidant mouthwashes by loading quercetin and mint essential oil into phospholipid vesicles.[141] Studies show that ethanol can increase systemic drug exposure by enhancing gastrointestinal absorption of poorly soluble drugs, suggesting a need for further research on its effects.[142]

However, ethanol can affect the digestive tract by slowing gastric emptying, stimulating gastric acid secretion, and increasing intestinal permeability, which may impact drug absorption and increase exposure to lipophilic drugs.[136]

Although ethanol is typically present in small amounts in medications, it can still pose risks to infants and young children, as evidenced by cases of toxicity from accidental exposure. Children metabolize ethanol differently from adults, with lower levels of key metabolic enzymes, making them more susceptible to its effects. Thus, it is crucial to monitor and regulate ethanol content in medicines to ensure the safety of pediatric patients.[137]

Ethanol in Herbal Medicinal

Ethanol is commonly used in herbal liquid formulations and OTC medicines, often promoted for their health benefits. It acts as an extractant to produce solid, liquid, or semi-concentrated herbal or animal-based preparations, as defined by the

European Pharmacopoeia 9th Edition.[143] Herbal medicines are regulated by the European Pharmacopoeia and other relevant documents, which classify herbal extracts based on their physical form—liquid, semi-solid, or solid. According to the European Pharmacopoeia, extracts can be categorized into standardized extracts, measured extracts, or other types of extracts.[144]

Ethanol precipitation is a method used to purify traditional herbal formulas. This technique exploits the fact that most bioactive compounds are more soluble in higher concentrations of ethanol, while contaminants are less soluble. By increasing the ethanol concentration, unwanted substances precipitate out, leaving a potent bioactive concentrate that can be used to create tablets or granules.

In terms of solvent regulation, Class 3 solvents, including acetone, ethanol, and ethyl acetate, are considered to have low toxic potential and do not require health-based exposure limits like Class 1 and 2 solvents. Studies show that Class 3 solvents are typically within acceptable concentration limits and do not exceed regulatory thresholds.[145]

Safety concerns have emerged regarding ethanol in herbal products for children.[146] Recent analyses reveal that nearly all tested products exceed WHO ethanol limits for different age groups: under 6 years (<0.5%), 6–12 years (<5%), and over 12 years (<10%). Some products even showed blood alcohol levels above toxicological limits, underscoring the need for stricter regulations on ethanol content.[147]

Given these concerns, experts recommend a comprehensive risk-benefit analysis to determine if the benefits of herbal products outweigh the risks associated with alcohol, especially for children. They also advise that producers in Belgium justify the use of alcohol in their products, accurately document ethanol content, and calculate alcohol intake based on recommended doses for different age groups. These measures aim to ensure safety and transparency in the use of herbal medicines containing alcohol.

Ethanol in Vinegar

Vinegar, a consumable liquid made from agricultural raw materials like starch and sugar, undergoes a double fermentation process involving alcohol and acetic acid.[148,149] It consists of acetic acid, water, and a mix of alcohols, acids, aldehydes, and ketones, and contains bioactives such as polyphenols, carotenoids, phytosterols, and vitamins C and E. Vinegar, used traditionally as a seasoning and preservative, offers benefits like improved digestion and antioxidant, antidiabetic, and antimicrobial properties.[149] It is produced from various sources including grapes, apple juice, honey, rice, and barley malt, with production in northeastern Asia often using cereals like rice. Key bacteria like *Acetobacter aceti* and yeasts such as *Saccharomyces cerevisiae* play crucial roles. Adding 10–25% strong vinegar to the alcohol substrate helps achieve optimal fermentation, influenced by factors such as temperature, yeast strain, and sugar and oxygen levels.[150]

Vinegar contains functional compounds like amino acids, sugars, vitamins, organic acids, phenolic substances, and bioactives such as lovastatin.[151] Research shows black vinegar has the highest ethanol content (3.21%), while traditionally produced Nipah vinegar has the lowest (1.70%). All tested samples exceeded the Malaysian National Fatwa Committee's ethanol limit of 1% v/v, highlighting the need for revised standards.[152] Ethanol levels in vinegar, whether halal-certified or not, show no significant difference. In Islam, vinegar with ≥1% ethanol is classified as khamr and is not consumable. Saudi Arabian vinegar has 0.0228% ethanol, and brand "x" in Surabaya has 0.0117%.[153] Khalas date vinegar, noted for its higher carotenoid content and antioxidant activity, demonstrates superior quality and production efficiency.[154]

Alcohol-Food Interaction

Consuming food before or with alcohol slows its absorption by delaying gastric emptying and boosting first-pass metabolism in the stomach and liver. A meal of about 700 kcal can reduce peak BAC and overall bioavailability by over 50%. However, such a large meal is often impractical, and current research indicates that total caloric intake is the main factor affecting alcohol absorption, rather than the type of food or macronutrients.[155] Consuming alcohol with high-protein foods can slow down the absorption of alcohol, resulting in a delayed but prolonged effect. Conversely, alcohol consumed with high-carbohydrate foods can accelerate alcohol absorption, increasing blood alcohol levels more rapidly. Alcohol can also stimulate stomach acid production, which can worsen conditions like gastritis or ulcers, especially when consumed with spicy or acidic foods. Long-term alcohol consumption can lead to deficiencies in essential nutrients such as thiamine (vitamin B1), folic acid, vitamin B12, vitamin A, calcium, and zinc, potentially causing anemia, nerve damage, and immune system dysfunction.[156–158]

Fermented foods like kimchi, sauerkraut, and certain cheeses contain tyramine. When consumed with alcohol, particularly red wine and beer, these can cause increased blood pressure and headaches in individuals sensitive to tyramine[159,160] Additionally, some herbal supplements, such as kava, valerian, and St. John's Wort, can interact with alcohol, enhancing sedative effects and increasing the risk of dizziness and confusion.[161,162] Combining alcohol with caffeine-containing beverages like coffee or energy drinks can mask alcohol's depressant effects, leading to increased alcohol consumption and a higher risk of alcohol poisoning and alcohol-related accidents.

Food-drug interactions are increasingly important in healthcare. According to the FDA, these interactions occur when food or drinks alter a drug's pharmacokinetics or pharmacodynamics, leading to unexpected effects. Such interactions can modify drug absorption, distribution, metabolism, and excretion, potentially causing adverse effects or new drug responses. Alcohol often interacts with various foods, altering their biological impact and raising harm risks. For instance, alcohol can reduce the effectiveness of anticoagulant medications when consumed with vitamin K-rich foods like broccoli and spinach, increasing stroke or heart attack risks. Additionally, pairing alcohol with foods such as ripe cheese or red grapes can cause hypertension in those using monoamine oxidase inhibitors (MAOIs).[112]

Alcohol also affects insulin or oral diabetes medications by prolonging their effect, which can result in low blood sugar.[163] Chronic alcohol consumption depletes hepatic glutathione, which helps neutralize N-acetyl- p -benzoquinonimine (NAPQI). Chronic alcohol use can induce cytochrome P450 enzymes in the liver, specifically, Cytochrome P450 2E1 (CYP2E1), facilitating an increased conversion of acetaminophen to NAPQI. Alcohol can contribute to a heightened inflammatory response in the liver. Acetaminophen-induced liver injury triggers an inflammatory cascade, and alcohol can exacerbate this process. Chronic alcohol consumption impairs the regenerative capacity of the liver, leading to delayed recovery and potentially more severe liver injury.[164] Additionally, taking antihistamines, such as Benadryl, with alcohol can increase drowsiness, making activities like driving dangerous.[165,166]

Consuming alcohol with dietary fat can exacerbate lipid peroxidation and elevate the production of reactive oxygen species. This can activate procarcinogens via cytochrome P4502E1 induction, resulting in DNA damage from oxidative stress.[167,168]

Halal Status of Ethanol

The global halal market is experiencing significant growth, driven by the increasing Muslim population, which is influencing various industries, including food, beverages, medicines, and cosmetics.[169,170] In response to this growth, since 1997, The FAO/WHO has set general guidelines for using the term "halal", outlining its scope, definition, criteria, and labelling requirements. These guidelines ensure that halal products comply with Islamic law, meaning they must be free from alcohol, intoxicating substances, harmful substances, and any additives derived from such substances.[120,171]

Religions and customs strongly influence food habits, often through dietary laws that reflect a community's heritage and socio-cultural identity. In Islam, halal refers to foods that are clean, safe, and permissible under Islamic law, while haram means forbidden. These dietary rules are essential expressions of religious and cultural values.[171] According to halal regulations and standards, there are some permissible (non-khamr) ethanol that can be present in food and beverage products.[120]

In Islamic teachings, the Qur'an refers to alcoholic beverages as "Khamr", mentioned six times, and describes them as solutions produced through the anaerobic fermentation of fruits or natural sugars. The main component of Khamr is ethanol, which is responsible for its intoxicating effects, including relaxation, euphoria, and impaired judgment. Building on these religious foundations, recent fatwas have introduced new considerations regarding ethanol in halal products. According to these rulings, the ethanol content in food products is not limited as long as it is not medically harmful. In contrast, ethanol in beverages is tolerated at levels below 0.5%, provided it is also not harmful. Additionally, ethanol in intermediate products like flavourings is not restricted, as long as its presence in the final product adheres to these guidelines.[11]

Permissible ethanol levels in halal products differ by country: the Islamic Food and Nutrition Council of America (IFANCA) sets a limit of under 0.1%, the Korea Muslim Federation (KMF) and Malaysia's JAKIM allow up to 0.5%, while Indonesia's Ulema Council (MUI) permits up to 1.0%. These variations highlight the diverse interpretations of Islamic law across different regions.[38]

Ethanol's halal status is determined by its source, concentration, and intended use. Ethanol concentrations below 1% are typically considered mubah (permissible) as they do not induce intoxication and are frequently used as food preservatives. For instance, vinegar containing up to 1% ethanol is deemed halal if not intended for intoxication. The MUI Fatwa No. 10 (2018) allows ethanol use in beverages up to 0.5% vol/vol, extending this allowance to low ethanol concentrations in food products that are not medically harmful.[11]

Ethanol derived from khamr (alcohol from grape fermentation) is prohibited due to its impurity, while ethanol from non-alcoholic sources, such as the natural fermentation of fruits, is permissible under specific conditions, especially at non-intoxicating concentrations in food and beverages. Industrial uses of ethanol, such as disinfection or as a raw material, are allowed even at concentrations above 15%, though such ethanol is considered toxic and unsuitable for consumption. Ethanol diluted from absolute or denatured ethanol is similarly restricted to industrial applications.[152]

In halal-certified products like spices and flavorings, ethanol is permissible if its final concentration does not exceed 0.1%. Ensuring compliance with halal guidelines, particularly concerning the ethanol source, is crucial for manufacturers targeting Muslim consumers. However, variations in halal standards across countries can complicate international compliance. Ongoing efforts to harmonize these standards aim to facilitate global trade in halal products while maintaining adherence to Islamic dietary laws.

A case study examined the application of halal standards in slaughterhouses by comparing four different certifications —GSO 993:2015, OIC/SMIIC 1:2019, HAS 23103:2012, and MS 1500:2019—across various regions. Achieving a consistent regulatory framework with unified certification and accreditation procedures necessitates close collaboration among the authorities issuing halal certifications, especially in a globalized market. (Table 4).[171]

Table 4 Halal Policies Related to Alcohol in Various Products Across Several Countries

Country	General Policy	Fermented Products	Pharmaceuticals	Beauty/Cosmetics Products	Soft Drinks	Ref
Malaysia (JAKIM)	Alcohol is prohibited for Muslims, except in small amounts that are not intoxicating in certain products.	Allows up to 1% alcohol from natural fermentation, provided it is not intoxicating.	Medicines and perfumes containing alcohol as a solvent agent are not impure and are permissible provided such alcohol is not extracted from the khamr making process.	Alcohol from non-khamr (non-wine) sources is allowed.	Allows up to 0.5%–-1% alcohol from natural fermentation, provided it is not intoxicating.	[92–94]
Indonesia (MUI)	Alcohol is prohibited for Muslims, but there is tolerance for small amounts in certain products.	Small amounts of alcohol (1%) from natural fermentation are allowed if not intoxicating.	Allowed in small amounts as a solvent with MUI approval.	Alcohol in cosmetics must come from non-khamr sources and is allowed if there are no other alternatives.	Allows up to 0.5% - 1% alcohol from natural fermentation, provided it is not intoxicating.	[93, 95]

(*Continued*)

Table 4 (Continued).

Country	General Policy	Fermented Products	Pharmaceuticals	Beauty/Cosmetics Products	Soft Drinks	Ref
Brunei Darussalam	Alcohol is strictly prohibited for Muslims, with exceptions for very small amounts that are not intoxicating.	Allows very small amounts of alcohol from natural fermentation (2%), provided it is not intoxicating.	Allowed if there are no other alternatives and used in small amounts.	Alcohol from non-khamr sources is allowed if there are no other alternatives.	Allows very small amounts of alcohol from natural fermentation, provided it is not intoxicating.	[93, 96]
Saudi Arabia	Alcohol is completely banned, with severe penalties for violators.	Natural fermentation that produces very small amounts of alcohol, which is not intoxicating, can be acceptable in certain contexts.	Allowed in special cases if there are no effective alternatives.	Very strict, but small amounts of alcohol from non-khamr sources can be permitted in cosmetics.	Very strict, soft drinks with alcohol are usually not allowed.	[97]

Perspective

Ethanol is commonly found in foods, but data on the health risks associated with low doses are limited. Although moderate alcohol consumption may have potential benefits, such as lowering the risk of diabetes and ischemic heart disease, these effects are not fully understood and may be attributed to non-ethanol components like polyphenols. While chronic alcoholism does not affect inflammatory bowel disease (IBD) risk, long-term abuse and binge drinking are associated with immunosuppression and increased infection risk. This raises concerns about the overall benefits of alcohol, leading some experts to recommend abstinence as the safest approach.[172]

The debate over low-dose ethanol consumption highlights both potential benefits and safety concerns. Research in animal models suggests that low-dose ethanol may improve liver function, reduce serum urate levels, and prevent obesity.[173] Specifically, 1% ethanol may help prevent colon tumorigenesis, supporting the J-curve hypothesis that low-dose alcohol could have health benefits by modulating gut bacteria and inflammatory markers.[174] However, ethanol exposure leads to chronic oxidative stress and immune dysfunction in the lungs, decreasing glutathione levels and impairing immune responses. In neonates, maternal alcohol use increases the risk of sepsis and respiratory infections. Studies show that treating ethanol-exposed neonatal mice with liposomal glutathione (LGSH) can reduce oxidative stress, restore immune function, and decrease infections and lung damage, indicating LGSH as a potential therapy for prenatal alcohol exposure effects.[175]

Animal studies suggest that low doses of ethanol may provide some health benefits, such as improved liver function and prevention of obesity. However, the application of these findings to humans should be approached with caution because the health effects of alcohol are complex and vary based on individual factors such as genetics and lifestyle. Ethanol is converted to acetaldehyde, a carcinogen that can harm DNA and elevate cancer risk, particularly in the upper gastrointestinal tract. Although light to moderate alcohol consumption might offer some benefits, the risks posed by acetaldehyde warrant caution. Our findings suggest that light to moderate drinking does not show significant benefits on the risk of hypertension and may even be harmful when compared with abstinence or high alcohol consumption.[52,53]

Although extensive evidence links excessive alcohol consumption to adverse cardiovascular changes and potential cardiomyopathy, key details remain unclear. Specifically, we lack precise information on who is at risk, the timing of onset, and the exact amount and duration of alcohol exposure needed to induce disease. Addressing these questions is crucial for identifying at-risk individuals, customizing treatments, preventing misdiagnoses, and curbing disease progression.[116]

While excessive alcohol is known to contribute to cardiovascular remodelling and cardiomyopathy, the precise amount and duration of exposure required to trigger these conditions remain unclear. This knowledge is vital for identifying at-risk individuals, customizing treatments, and preventing disease. Although reducing alcohol intake can benefit cardiovascular patients, there is no universally safe level of consumption, and those with arrhythmias should avoid alcohol altogether.[56,57] Evidence on alcohol's impact on various arrhythmias is mixed, emphasizing the need for moderation and further research to determine safe consumption levels and individual risk factors. Abstaining from alcohol can help restore health in affected patients.[61]

The conversion of ethanol to acetaldehyde, a known carcinogen, further complicates the safety of ethanol in foods. Synthetic alcohols and naturally fermented alcohols differ significantly in their production processes and properties. Synthetic alcohols are produced through chemical reactions with raw materials like ethylene, resulting in highly pure products with controlled quality. Conversely, naturally fermented alcohols are derived from the fermentation of sugars by microorganisms, yielding alcohol with organic byproducts. While synthetic alcohols are widely used in industry due to their purity, naturally fermented alcohols are considered more natural and can be acceptable in a halal context if they meet halal standards. Both types of alcohol must comply with halal regulations to adhere to halal principles.

Comprehensive guidelines are needed to address the composition, measurement, production, and regulation of alcoholic beverages across different regions. These guidelines should tackle the variability in alcohol content, challenges in measurement standards, and the importance of clear labelling and consumer information. Additionally, public health risks associated with potential methanol contamination in ethanol or isopropyl alcohol underscore the need for vigilance. Consequently, the halal food community must verify the levels of natural ethanol in products like soft drinks and fruits and ensure that halal product labels accurately reflect alcohol content.[128]

A study has highlighted the hepatoprotective benefits of a mixture containing fermented *Schizandrae Fructus pulp* and *Hoveniae Semen cum* Fructus (MSH) against liver damage caused by ethanol. MSH has been shown to improve hepatic steatosis, inflammation, and oxidative stress by modulating lipid metabolism, reducing inflammatory cytokines, and enhancing antioxidant defenses. These results imply that MSH may offer a valuable approach for both preventing and managing alcoholic liver disease.[117]

The growing demand for halal products is prompting manufacturers to adhere to varying halal standards for competitive advantage. However, the lack of a universally recognized certification due to differing requirements from various certifying bodies complicates matters. Establishing a unified global halal standard and a consistent monitoring system would streamline trade and build greater confidence among producers and consumers.

Despite efforts to harmonize existing standards, unification remains elusive. It is important to include alcohol information as in Table 5, to provide consumers with the flexibility to make purchasing decisions. Collaboration between certification authorities across countries is essential to building a consistent regulatory framework, which is increasingly needed in the global marketplace.

Table 5 Alcohol Descriptors Guidance

Descriptor	Conditions	Labelling Requirements
Alcohol Free	Non-alcoholic beverages contain less than 0.05% alcohol after extraction process.	Products must display alcohol content or "no alcohol" label.
De-alcoholyses	Non-alcoholic beverages contain less than 0.05% alcohol after extraction process.	Products must display alcohol content or "no alcohol" label.
Non-alcoholic	Cannot use alcoholic drink names except for non-alcoholic communion wine.	Must label if intended for religious/sacramental use.
Low Alcohol	Product must contain 1.2% or less alcohol content.	Label must display maximum alcohol content (1.2% ABV).

Conclusion

Ethanol is a widely used bioactive compound found in a variety of foods, pharmaceuticals, cosmetics, and industrial products. Despite its widespread use, there is no safe level of alcohol consumption, as defined by the World Health Organization. Studies have linked small levels of ethanol to several health risks, including chronic disease, neurotoxicity, and potential carcinogenic effects, which are exacerbated by its often-unacknowledged presence in many products. These health risks have a significant impact on vulnerable populations and contribute to a large economic burden through lost productivity and health care costs. Therefore, there is a critical need for comprehensive public health strategies and stringent regulatory measures to manage the presence of ethanol in consumer products, particularly from countries with significant Muslim populations, to safeguard public health, respect cultural practices, and effectively address economic impacts. In this review we have clear Ethanol's halal status is determined by its source, concentration, and intended use. Further research is needed to develop improved detection methods, study health impacts of trace ethanol exposure, establish standardized labelling requirements, and find alternative preservation techniques while examining economic impacts of regulations and cultural needs for ethanol-free alternatives.

Data Sharing Statement

No data was used for the research described in the article.

Ethics Approval and Consent to Participate

This research did not involve human participants, human data, or human tissue. As such, ethical approval and consent to participate were not applicable.

Disclosure

The author declares no conflicts of interest.

References

1. Ramsbottom A, van Schalkwyk MCI, Carters-White L, Benylles Y, Petticrew M. Food as harm reduction during a drinking session: reducing the harm or normalising harmful use of alcohol? A qualitative comparative analysis of alcohol industry and non-alcohol industry-funded guidance. *Harm Reduction Journal*. 2022;19(1):1–9. doi:10.1186/s12954-022-00648-y
2. Hans M, Lugani Y, Chandel AK, Rai R, Kumar S. Production of first- and second-generation ethanol for use in alcohol-based hand sanitizers and disinfectants in India. *Biomass Convers Bioref*. 2023;13(9):7423–7440. doi:10.1007/s13399-021-01553-3
3. Tse TJ, Wiens DJ, Chicilo F, Purdy SK, Reaney MJT. Value-Added Products from Ethanol Fermentation — a Review. *Fermentation*. 2021;7 (267):1–19.
4. Voidarou C, Antoniadou M, Rozos G, et al. Fermentative foods: microbiology, biochemistry, potential human health benefits and public health issues. *Foods*. 2021;10(1):1–27. doi:10.3390/foods10010069
5. Terracina S, Tarani L, Ceccanti M, et al. The Impact of Oxidative Stress on the Epigenetics of Fetal Alcohol Spectrum Disorders. *Antioxidants*. 2024;13(410):1–16.
6. Surma S, Gajos G. Alcohol, health loss, and mortality: can wine really save the good name of moderate alcohol consumption? *Polish Arch Intern Med*. 2024;134(4). doi:10.20452/pamw.16708
7. Derme M, Piccioni MG, Brunelli R, et al. Oxidative Stress in a Mother Consuming Alcohol during Pregnancy and in Her Newborn: a Case Report. *Antioxidants*. 2023;12(1216):1–11.
8. Subramaniyan V, Chakravarthi S, Jegasothy R, et al. Alcohol-associated liver disease: a review on its pathophysiology, diagnosis and drug therapy. *Toxicol Reports*. 2021;8(August 2020):376–385. doi:10.1016/j.toxrep.2021.02.010
9. Xu F, Sun D, Wang Z, et al. Highly Efficient Production of Cellulosic Ethanol from Poplar Using an Optimal C6 / C5 Co-Fermentation Strain of Saccharomyces cerevisiae. *Microorganisms*. 2024;12(1174):1–17.
10. Tse TJ, Wiens DJ, Reaney MJT. Production of Bioethanol—A Review of Factors Affecting Ethanol Yield. *Fermentation*. 2021;7(4):1–18. doi:10.3390/fermentation7040268
11. Alzeer J, Abou Hadeed K. Ethanol and its Halal status in food industries. *Trends Food Sci Technol*. 2016;58(September):14–20. doi:10.1016/j.tifs.2016.10.018
12. Baharum NB, Daud awang M, Arshad S, Abd Gani SS. A Study of Literatures: status of Alcohol in Cosmetics Products from Shariah Views in Malaysia. *KnE Soc Sci*. 2020;2020:379–393. doi:10.18502/kss.v4i9.7338
13. Gupta R, Badhe Y, Rai B, Mitragotri S. Molecular mechanism of the skin permeation enhancing effect of ethanol: a molecular dynamics study. *RSC Adv*. 2020;10(21):12234–12248. doi:10.1039/d0ra01692f
14. Kalathenos P, Russell NJ. Ethanol as a food preservative. *Food Preserv*. 2003;vIv)196–217. doi:10.1007/978-0-387-30042-9_10
15. Chapp AD, Shan Z. Acetic Acid: an Underestimated Metabolite in Ethanol-Induced Changes in Regulating Cardiovascular Function. *Antioxidants*. 2024;13(139):1–19.

16. Hartz SM, Oehlert M, Horton A, et al. Daily drinking is associated with increased mortality. *Hhs Public Access*. 2019;123(11):40–43. doi:10.1111/acer.13886.Daily
17. Im PK, Wright N, Yang L, et al. Alcohol consumption and risks of more than 200 diseases in Chinese men. *Nat Med*. 2023;29(6):1476–1486. doi:10.1038/s41591-023-02383-8
18. Burton R, Sheron N. No level of alcohol consumption improves health. *Lancet*. 2018;392(10152):987–988. doi:10.1016/S0140-6736(18)31571-X
19. Anderson BO, Berdzuli N, Ilbawi A, et al. Health and cancer risks associated with low levels of alcohol consumption. *Lancet Public Heal*. 2023;8(1):e6–e7. doi:10.1016/S2468-2667(22)00317-6
20. Kalelkar A, Sipe G, Castro E Costa AR, et al. A paradigm for ethanol consumption in head-fixed mice during prefrontal cortical two-photon calcium imaging. *Neuropharmacology*. 2024;245. doi:10.1016/j.neuropharm.2023.109800
21. Watson MR, James K, Mittleman G, Matthews DB. Impact of acute ethanol exposure on body temperatures in aged, adult and adolescent male rats. *Alcohol*. 2020;82:81–89. doi:10.1016/j.alcohol.2019.08.001
22. Sutanto H, Cluitmans MJM, Dobrev D, Volders PGA, Bébarová M, Heijman J. Acute effects of alcohol on cardiac electrophysiology and arrhythmogenesis: insights from multiscale in silico analyses. *J Mol Cell Cardiol*. 2020;146:69–83. doi:10.1016/j.yjmcc.2020.07.007
23. Forward P. Economic Research on Ethanol Feed-Use Coproducts: a Review, Synthesis, and Path Forward. *Animals*. 2024;14(1551):1–21.
24. Chen L, Debnath D, Zhong J, Ferin K, VanLoocke A, Khanna M. The economic and environmental costs and benefits of the renewable fuel standard. *Environ Res Lett*. 2021;16(3). doi:10.1088/1748-9326/abd7af
25. Araghi MK, Barkhordari S, Hasannia R. Economic impacts of producing bioethanol in Iran: a CGE approach. *Energy*. 2023;263(PC):125765. doi:10.1016/j.energy.2022.125765
26. Tomkins MM, Wang C, Weinstein A, Neighbors C, DiBello AM, Carey KB. Religion and drinking: differences between two campuses. *Alcohol*. 2023;110:41–49. doi:10.1016/j.alcohol.2023.01.005
27. Sisco E, Robinson EL. Determination of ethanol concentration in alcoholic beverages by direct analysis in real time mass spectrometry (DART-MS). *Forensic Chem*. 2020;18. doi:10.1016/j.forc.2020.100219
28. Phongphakdee K, Nitisinprasert S. Combination Inhibition Activity of Nisin and Ethanol on the Growth Inhibition of Pathogenic Gram Negative Bacteria and Their Application as Disinfectant Solution. *J Food Sci*. 2015;80(10):M2241–6. doi:10.1111/1750-3841.13015
29. Collins SE, Kirouac M. Alcohol Consumption BT - Encyclopedia of Behavioral Medicine. In: Gellman MD, Turner JR, editors. *Alcohol Consumption*. Springer New York; 2013:61–65. doi:10.1007/978-1-4419-1005-9_626
30. Oh J, Kim MK. Effect of alternative preservatives on the quality of rice cakes as halal food. *Foods*. 2021;10(10):1–9. doi:10.3390/foods10102291
31. Yun Y. Alcohol Fuels: current Status and Future Direction. In: Yun Y, editor. *Alcohol Fuels: Current Status and Future Direction*. IntechOpen;2020:1. doi:10.5772/intechopen.89788
32. Gomes AM. Chapter 10 - Intervention in the preservation and collection of evidences. In: editor. *EMS Crime Scene*. 2021:133–173. doi:10.1016/B978-0-12-824420-3.00011-3
33. Ethanol N halal C, Using P, Quantum YL. Analisa Kandungan Non Halal (Kadar Ethanol) Pada Peuyeum Menggunakan Gas Chromatography YL6500 Quantum Terhadap Metode Validasi. In: *Seminar Nasional Hasil-Hasil Penelitian Dan Pengabdian Masyarakat*. 2022:1.
34. Speight JG. Distillation. In: editor. *The Refinery of the Future*. Gulf Professional Publishing;2020:125–159. doi:10.1016/B978-0-12-816994-0.00004-X
35. Sun W, Li X, Zhao J. Pretreatment Strategies to Enhance Enzymatic Hydrolysis and Cellulosic Ethanol Production for Biorefinery of Corn Stover. *Int J Mol Sci*. 2022;23(13163):1–15.
36. Paula A, Sica P, De Almeida L, et al. Integration of Corn and Cane for Ethanol Production: effects of Lactobacilli Contamination on Fermentative Parameters and Use of Ionizing Radiation Treatment for Disinfection. *Fermentation*. 2023;8(89):1–13.
37. Sources L, Vasi K. Bioethanol Production by Enzymatic Hydrolysis from Different. *Molecules*. 2021;26(753):1–23.
38. Kim Y, Shim YS, Lee KG. Determination of alcohols in various fermented food matrices using gas chromatography-flame ionization detector for halal certification. *Food Sci Biotechnol*. 2022;31(13):1639–1646. doi:10.1007/s10068-022-01156-2
39. Palacios-vel A, Quispe-coquil V, Mart E. Acquisition, Characterization, and Optimization of Distilled Bioethanol Generated from Fermented Carrot (Daucus carota) Residues. *Fermentation*. 2023;9(867):1–13.
40. Tse TJ, Purdy SK, Shen J, et al. Toxicology of alcohol-based hand rubs formulated with technical-grade ethanol. *Toxicol Reports*. 2021;8:785–792. doi:10.1016/j.toxrep.2021.03.034
41. Abuga K, Nyamweya N. Alcohol-Based Hand Sanitizers in COVID-19 Prevention: a Multidimensional Perspective. *Pharmacy*. 2021;9(1):64. doi:10.3390/pharmacy9010064
42. Tsafara P, Passadis K, Christianides D, et al. Advanced Bioethanol Production from Source-Separated Bio-waste in Pilot Scale. *Sustain*. 2022;14(19). doi:10.3390/su141912127
43. dung HT, Nghiem N. Recent Developments and Current Status of Commercial Production of Fuel Ethanol. *ferme*. 2021;7(314):1–18.
44. Tesfaw A, Oner ET, Assefa F. Optimization of ethanol production using newly isolated ethanologenic yeasts. *Biochem Biophys Reports*. 2021;25:100886. doi:10.1016/j.bbrep.2020.100886
45. Navianti D, Tarmizi MI, Holifah SN. The Presence of Methanol in Alcoholic Beverages Analyzed Using Qualitative Method. *J Teknol Lab*. 2018;7(2):46–52. doi:10.29238/teknolabjournal.v7i1.117
46. Marques JC, Gasi F, Lourenço SR. Biofuel in the Automotive Sector: viability of Sugarcane Ethanol. *Sustain*. 2024;16(7). doi:10.3390/su16072674
47. Hassani N. The reaction mechanism of the hydration of ethylene over the CorroleM (M = B, Al, and Ga) complexes: a theoretical approach. *Comput Theor Chem*. 2020;1177:112766. doi:10.1016/j.comptc.2020.112766
48. Liu SY, Tsai IT, Hsu YC. Alcohol-related liver disease: basic mechanisms and clinical perspectives. *Int J Mol Sci*. 2021;22(10). doi:10.3390/ijms22105170
49. Roerecke M, Vafaei A, Hasan OS, et al. Alcohol consumption and risk of liver cirrhosis: a systematic review and meta-analysis. *Am J Gastroenterol*. 2019;114(10):1574–1586. doi:10.4049/jimmunol.1801473
50. Yoshiji H, Nagoshi S, Akahane T, et al. Evidence-based clinical practice guidelines for Liver Cirrhosis 2020. *J Gastroenterol*. 2021;56(7):593–619. doi:10.1007/s00535-021-01788-x

51. Okojie OM, Javed F, Chiwome L, Hamid P. Hypertension and Alcohol: a Mechanistic Approach. *Cureus*. 2020;12(8):1–7. doi:10.7759/cureus.10086
52. Cecchini M, Filippini T, Whelton PK, et al. Alcohol Intake and Risk of Hypertension: a Systematic Review and Dose-Response Meta-Analysis of Nonexperimental Cohort Studies. *Hypertension*. 2024;81(8):1701–1715. doi:10.1161/HYPERTENSIONAHA.124.22703
53. Fuchs FD, Fuchs SC. The Effect of Alcohol on Blood Pressure and Hypertension. *Curr Hypertens Rep*. 2021;23(10):42. doi:10.1007/s11906-021-01160-7
54. Maisch B. Alkoholische Kardiomyopathie: eine Folge der Dosis und der individuellen Prädisposition [Alcoholic cardiomyopathy: The result of dosage and individual predisposition]. *Herz*. 2016;41(6):484–493. doi:10.1007/s00059-016-4469-6
55. Ihekire NL, Okobi OE, Adedoye EA, et al. Heartache in a Bottle: understanding Alcoholic Cardiomyopathy. *Cureus*. 2023;15(8). doi:10.7759/cureus.42886
56. Wong CX, Tu SJ, Marcus GM. Alcohol and Arrhythmias. *JACC Clin Electrophysiol*. 2023;9(2):266–279. doi:10.1016/j.jacep.2022.10.023
57. Day E, Rudd JHF. Alcohol use disorders and the heart. *Addiction*. 2019;114(9):1670–1678. doi:10.1111/add.14703
58. Mulorz J, Ibing W, Cappallo M, et al. Ethanol Enhances Endothelial Rigidity by Targeting VE-Cadherin — implications for Acute Aortic Dissection. *J Clin Med*. 2023;12(4967):1–12.
59. Xu J, Xu S, Luo J, et al. Epigallocatechin-3-gallate Alleviates Ethanol-Induced Endothelia Cells Injury Partly through Alteration of NF-κB Translocation and Activation of the Nrf2 Signaling Pathway. *Biol Pharm Bull*. 2024;47(7):1248–1254. doi:10.1248/bpb.b23-00773
60. Adejumo AC, Li J, Akanbi O, Adejumo KL, Bukong TN. Reduced Prevalence of Alcoholic Gastritis in Hospitalized Individuals Who Consume Cannabis. *Alcohol Clin Exp Res*. 2019;43(2):270–276. doi:10.1111/acer.13930
61. Rajan AK, Jeyamani VP, Sabishruthi S, et al. Alcoholic gastritis: eminence of clinical pharmacist to attenuate quality of life. *Int J Pharm Clin Res*. 2019;11(3):90–93.
62. Miksch RC, D'Haese JG, Werner J. Surgical Therapy of Chronic Alcoholic Pancreatitis: a Literature Review of Current Options. *Visc Med*. 2020;36(3):191–197. doi:10.1159/000508174
63. Chen Y, Chen C, Ouyang Z, et al. Prevalence and beverage-related risk factors of gastroesophageal reflux disease: an original study in Chinese college freshmen, a systemic review and meta-analysis. *Neurogastroenterol Motil*. 2022;34(5):e14266. doi:10.1111/nmo.14266
64. Sadafi S, Azizi A, Pasdar Y, Shakiba E, Darbandi M. Risk factors for gastroesophageal reflux disease: a population-based study. *BMC Gastroenterol*. 2024;24(1):64. doi:10.1186/s12876-024-03143-9
65. Pan J, Cen L, Chen W, Yu C, Li Y, Shen Z. Alcohol Consumption and the Risk of Gastroesophageal Reflux Disease: a Systematic Review and Meta-analysis. *Alcohol Alcohol*. 2019;54(1):62–69. doi:10.1093/alcalc/agy063
66. Maccioni L, Fu Y, Horsmans Y, et al. Alcohol-associated bowel disease: new insights into pathogenesis. *eGastroenterology*. 2023;1(1):e100013. doi:10.1136/egastro-2023-100013
67. Ramos GP, Kane S. Alcohol use in patients with inflammatory bowel disease. *Gastroenterol Hepatol*. 2021;17(5):221–225.
68. Oudman E, Wijnia JW, Oey MJ, van Dam M, Postma A. Wernicke-Korsakoff syndrome despite no alcohol abuse: a summary of systematic reports. *J Neurol Sci*. 2021;426(May):117482. doi:10.1016/j.jns.2021.117482
69. Schrader M, Bamborschke S, Lenk U, Sterr A. Case Report: intensive Inpatient Neurorehabilitation Achieves Sustained Real-World Benefits in Severe Alcohol-Related Wernicke-Korsakoff Syndrome: a Case Study With 7-Years Follow-Up. *Front Psychol*. 2021;12(June):1–8. doi:10.3389/fpsyg.2021.693920
70. Tessitore ME, Da S pereira-rufino L, Panfilio CE, et al. Alcoholic neuropathy associated with chronic alcohol intake. *IBRO Neurosci Reports*. 2022;13(August):177–186. doi:10.1016/j.ibneur.2022.08.004
71. Papantoniou M, Rentzos M, Zampelis T, Tzavellas E, Paparrigopoulos T, Kokotis P. Alcohol-related peripheral neuropathy: clinico-neurophysiological characteristics and diagnostic utility of the neuropathy symptoms score and the neuropathy impairment score. *Alcohol*. 2024;117:65–71. doi:10.1016/j.alcohol.2024.04.001
72. Jeon KH, Han K, Jeong SM, et al. Changes in Alcohol Consumption and Risk of Dementia in a Nationwide Cohort in South Korea. *JAMA Network Open*. 2023;6(2):e2254771. doi:10.1001/jamanetworkopen.2022.54771
73. Zahr NM. Alcohol Use Disorder and Dementia: a Review. *Alcohol Res Curr Rev*. 2024;44(1). doi:10.35946/arcr.v44.1.03
74. McCabe CJ, Brumback T, Brown SA, Meruelo AD. Assessing cross-lagged associations between depression, anxiety, and binge drinking in the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) study. *Drug Alcohol Depend*. 2023;243:109761. doi:10.1016/j.drugalcdep.2022.109761
75. Nunes EV. Alcohol and the Etiology of Depression. *Am J Psychiatry*. 2023;180(3):179–181. doi:10.1176/appi.ajp.20230004
76. Parker Gregg L, Susan hedayati S. Chapter 5 - Psychological challenges and psychiatric illness in earlier stages of CKD. In: Cukor D, Cohen SD, editors. *Psychosocial Aspects of Chronic Kidney Disease*. Academic Press; 2021:91–116. doi:10.1016/B978-0-12-817080-9.00005-1
77. Celik M, Gold MS, Fuehrlein B. A Narrative Review of Current and Emerging Trends in the Treatment of Alcohol Use Disorder. *Brain Sci*. 2024;14(3). doi:10.3390/brainsci14030294
78. Ferraguti G, Terracina S, Petrella C, et al. Alcohol and Head and Neck Cancer: updates on the Role of Oxidative Stress, Genetic, Epigenetics, Oral Microbiota, Antioxidants, and Alkylating Agents. *Antioxidants (Basel, Switzerland)*. 2022;11(1). doi:10.3390/antiox11010145
79. Kwon MJ, Kang HS, Choi HG, et al. Risk for Esophageal Cancer Based on Lifestyle Factors–Smoking, Alcohol Consumption, and Body Mass Index: insight from a South Korean Population Study in a Low-Incidence Area. *J Clin Med*. 2023;12(22). doi:10.3390/jcm12227086
80. Ndebia EJ, Kamsu GT. Drinking patterns, alcoholic beverage types, and esophageal cancer risk in Africa: a comprehensive systematic review and meta-analysis. *Front Oncol*. 2023;13(December):1–13. doi:10.3389/fonc.2023.1310253
81. Jacob R, Prince DS, Kench C, Liu K. Alcohol and its associated liver carcinogenesis. *J Gastroenterol Hepatol*. 2023;38(8):1211–1217. doi:10.1111/jgh.16248
82. Fu Y, Maccioni L, Wang XW, Greten TF, Gao B. Alcohol-associated liver cancer. *Hepatology*. 2024;2024:1.
83. Tran TPT, Han M, Luu NM, Oh JK. Alcoholic liver disease in relation to cancer incidence and mortality: findings from a large, matched cohort study in South Korea. *Cancer Med*. 2023;12(7):8754–8766. doi:10.1002/cam4.5614
84. Starek-świechowicz B, Budziszewska B, Starek A. Alcohol and breast cancer. *Pharmacol Rep*. 2023;75(1):69–84. doi:10.1007/s43440-022-00426-4

85. Young KL, Olshan AF, Lunetta K, et al. Influence of alcohol consumption and alcohol metabolism variants on breast cancer risk among Black women: results from the AMBER consortium. *Breast Cancer Res*. 2023;25(1):1–11. doi:10.1186/s13058-023-01660-1
86. Sapkota R, Zakaria J, Glenn E, et al. Alcohol Use and the Risk of Colorectal Liver Metastasis: a Systematic Mapping Review. *Biology*. 2023;12 (2). doi:10.3390/biology12020257
87. Chen X, Li H, Guo F, Hoffmeister M, Brenner H. Alcohol consumption, polygenic risk score, and early- and late-onset colorectal cancer risk. *eClinicalMedicine*. 2022;49:101460. doi:10.1016/j.eclinm.2022.101460
88. Varghese J, Dakhode S. Effects of Alcohol Consumption on Various Systems of the Human Body: a Systematic Review. *Cureus*. 2022;14 (10):8–13. doi:10.7759/cureus.30057
89. Tharmalingam J, Gangadaran P, Rajendran RL, Ahn BC. Impact of Alcohol on Inflammation, Immunity, Infections, and Extracellular Vesicles in Pathogenesis. *Cureus*. 2024;16(3). doi:10.7759/cureus.56923
90. Nguyen-Thanh T, Hoang-Thi AP, Anh Thu DT. Investigating the association between alcohol intake and male reproductive function: a current meta-analysis. *Heliyon*. 2023;9(5):e15723. doi:10.1016/j.heliyon.2023.e15723
91. Takure AO, Adewumi BA. Erectile Dysfunction among Male Infertile Men Attending the Surgical Outpatient Clinic in a Tertiary Hospital in Nigeria over a 7-Year Period—A Single Surgeon's Experience. *Eur J Clin Med*. 2023;4(5):31–34. doi:10.24018/clinicmed.2023.4.5.311
92. Lee PM, Xu X, Du JB, Li J. Paternal Preconceptional Alcohol Use Disorder With the Offspring's Mortality Risk. *Am J Prev Med*. 2024;67 (1):105–113. doi:10.1016/j.amepre.2024.02.017
93. Godos J, Giampieri F, Chisari E, et al. Alcohol Consumption, Bone Mineral Density, and Risk of Osteoporotic Fractures: a Dose–Response Meta-Analysis. *Int J Environ Res Public Health*. 2022;19(3). doi:10.3390/ijerph19031515
94. Johnson JT, Hussain MA, Cherian KE, Kapoor N, Paul TV. Chronic alcohol consumption and its impact on bone and metabolic health - A narrative review. *Indian J Endocrinol Metab*. 2022;26(3):206–212. doi:10.4103/ijem.ijem_26_22
95. Ke Y, Hu H, Zhang J, et al. Alcohol Consumption and Risk of Fractures: a Systematic Review and Dose–Response Meta-Analysis of Prospective Cohort Studies. *Adv Nutr*. 2023;14(4):599–611. doi:10.1016/j.advnut.2023.03.008
96. Khiyali Z, Rashedi V, Tavacol Z, Dehghan A, Bijani M. Smoking, alcohol consumption, drug abuse, and osteoporosis among older adults: a cross-sectional study on PERSIAN cohort study in Fasa. *BMC Geriatr*. 2024;24(1):1–8. doi:10.1186/s12877-024-04678-y
97. Bourgeois BL, Levitt DE, Molina PE, Simon L. Chronic Alcohol and Skeletal Muscle. In: Patel VB, Preedy VR, editors. *Handbook of Substance Misuse and Addictions: From Biology to Public Health*. Springer International Publishing; 2021:1–26. doi:10.1007/978-3-030-67928-6_49-1
98. Simon L, Bourgeois BL, Molina PE. Alcohol and Skeletal Muscle in Health and Disease. *Alcohol Res Curr Rev*. 2023;43(1). doi:10.35946/arcr.v43.1.04
99. Zhakubayev A, Sattgast LH, Lewis AD, et al. Ethanol consumption in non-human primates alters plasma markers of bone turnover but not tibia architecture. *Sci Rep*. 2024;14(1):1–10. doi:10.1038/s41598-024-65021-4
100. Lu T, Nakanishi T, Yoshiji S, Butler-Laporte G, Greenwood CMT, Richards JB. Dose-dependent Association of Alcohol Consumption With Obesity and Type 2 Diabetes: Mendelian Randomization Analyses. *J Clin Endocrinol Metab*. 2023;108(12):3320–3329. doi:10.1210/clinem/dgad324
101. Cao C, Wei C, Han Y, et al. Association between excessive alcohol consumption and incident diabetes mellitus among Japanese based on propensity score matching. *Sci Rep*. 2024;14(1):1–11. doi:10.1038/s41598-024-68202-3
102. Jayaprakash J, Siddabasave SG, K. Shukla P, et al. Sex-Specific Effect of Ethanol on Colon Content Lipidome in a Mice Model Using Nontargeted LC/MS. *ACS Omega*. 2024;9(14):16044–16054. doi:10.1021/acsomega.3c09597
103. Kearney N, Kirby B. Alcohol and Psoriasis for the Dermatologist: know, Screen, Intervene. *Am J Clin Dermatol*. 2022;23(6):881–890. doi:10.1007/s40257-022-00713-z
104. Liu L, Chen J. Advances in Relationship Between Alcohol Consumption and Skin Diseases. *Clin Cosmet Invest Dermatol*. 2023;16 (December):3785–3791. doi:10.2147/CCID.S443128
105. Diaz MR, Johnson JM, Varlinskaya EI. Increased ethanol intake is associated with social anxiety in offspring exposed to ethanol on gestational day 12. *Behav Brain Res*. 2020;393(June):112766. doi:10.1016/j.bbr.2020.112766
106. Freudenheim JL, Ph D, Abnet CC, et al. The IARC Perspective on Alcohol Reduction or Cessation and Cancer Risk. *N Engl J Med*. 2023;398 (26):2486–2494.
107. Cartus AT, Lachenmeier DW, Guth S, et al. Acetaldehyde as a Food Flavoring Substance: aspects of Risk Assessment. *Mol Nutr Food Res*. 2023;67(23). doi:10.1002/mnfr.202200661
108. Flashner S, Shimonosono M, Tomita Y, et al. ALDH2 dysfunction and alcohol cooperate in cancer stem cell enrichment. *Carcinogenesis*. 2024;45(1–2):95–106. doi:10.1093/carcin/bgad085
109. Belfiore CI, Galofaro V, Cotroneo D, et al. A Multi-Level Analysis of Biological, Social, and Psychological Determinants of Substance Use Disorder and Co-Occurring Mental Health Outcomes. *Psychoactives*. 2024;3(2):194–214. doi:10.3390/psychoactives3020013
110. Peng Q, Gilder DA, Bernert RA, Karriker-Jaffe KJ, Ehlers CL. Genetic factors associated with suicidal behaviors and alcohol use disorders in an American Indian population. *Mol Psychiatry*. 2024;29(4):902–913. doi:10.1038/s41380-023-02379-3
111. Wilson SE, Garcia K, Fava NM, Leeman RF. Examining the Relationships Among Adverse Experiences, Impulsivity, and Alcohol Use: a Scoping Review of Recent Literature. *Curr Addict Reports*. 2024;11(2):210–228. doi:10.1007/s40429-024-00552-4
112. Snr WS, Bashatah A, Al-Rawi MBA. Evaluation of Knowledge of Food–Drug and Alcohol–Drug Interactions Among Undergraduate Students at King Saud University – an Observational Study. *J Multidiscip Healthc*. 2022;15(November):2623–2633. doi:10.2147/JMDH.S391363
113. Dharavath RN, Pina-Leblanc C, Tang VM, et al. GABAergic signaling in alcohol use disorder and withdrawal: pathological involvement and therapeutic potential. *Front Neural Circuits*. 2023;17(October):1–19. doi:10.3389/fncir.2023.1218737
114. Su J, Wang P, Zhou W, et al. Single-site iron-anchored amyloid hydrogels as catalytic platforms for alcohol detoxification. *Nat Nanotechnol*. 2024. doi:10.1038/s41565-024-01657-7
115. Clauss NJ, Mayer FP, Owens WA, et al. Ethanol inhibits dopamine uptake via organic cation transporter 3: implications for ethanol and cocaine co-abuse. *Mol Psychiatry*. 2023;28(7):2934–2945. doi:10.1038/s41380-023-02064-5
116. Andersson C, Schou M, Gustafsson F, Torp-Pedersen C. Alcohol Intake in Patients With Cardiomyopathy and Heart Failure: consensus and Controversy. *Circ Hear Fail*. 2022;15(8):E009459. doi:10.1161/CIRCHEARTFAILURE.121.009459

117. Hwan JK, rim PH, rak CB, Kwang KJ. Synergistic Protective Effect of Fermented Schizandrae Fructus Pomace and Hoveniae Semen cum Fructus Extracts Mixture in the Ethanol-Induced Hepatotoxicity. *Antioxidants*. 2023;12(1602):1–17.
118. Gürler M, Bayram B. Estimation of ethanol and methanol exposure through jarred fruit purees. *Ann Ist Super Sanita*. 2023;59(4):260–266. doi:10.4415/ANN_23_04_04
119. Marek E, Kraft WK. Ethanol Pharmacokinetics in Neonates and Infants. *Curr Ther Res*. 2014;76:90–97. doi:10.1016/j.curtheres.2014.09.002
120. Mansur AR, Oh J, Lee HS, Oh SY. Determination of ethanol in foods and beverages by magnetic stirring-assisted aqueous extraction coupled with GC-FID: a validated method for halal verification. *Food Chem*. 2022;366(July):130526. doi:10.1016/j.foodchem.2021.130526
121. Drummer OH. Alcohol Congeners and the Source of Ethanol. In: Siegel JA, Saukko PJ, editors. *Encyclopedia of Forensic Sciences*. Academic Press; 2013:318–322. doi:10.1016/B978-0-12-382165-2.00297-X
122. Jain A, De S. 15 - Processing of Beverages by Membranes. In: Grumezescu AM, editor. *Processing and Sustainability of Beverages*. Woodhead Publishing; 2019:517–560. doi:10.1016/B978-0-12-815259-1.00015-X
123. Arslan M, Tahir HE, Zareef M, et al. Recent trends in quality control, discrimination and authentication of alcoholic beverages using nondestructive instrumental techniques. *Trends Food Sci Technol*. 2021;107(May 2020):80–113. doi:10.1016/j.tifs.2020.11.021
124. Pérez-Jiménez F, Pascual V, Meco JF, et al. Document of recommendations of the SEA 2018. Lifestyle in cardiovascular prevention. *Clínica e Investig En Arterioscler (English Ed*. 2018;30(6):280–310. doi:10.1016/j.artere.2018.11.001
125. Mestre MV, Maturano YP, Gallardo C, et al. Impact on sensory and aromatic profile of low ethanol Malbec wines fermented by sequential culture of Hanseniaspora uvarum and Saccharomyces cerevisiae native yeasts. *Fermentation*. 2019;5(3). doi:10.3390/fermentation5030065
126. Harrison NJ, Norris CA, Bartram A, et al. "They start on the zero-alcohol and they wanna try the real thing": parents' views on zero-alcohol beverages and their use by adolescents. *Aust N Z J Public Health*. 2024;48(3):100119. doi:10.1016/j.anzjph.2023.100119
127. Reimann H, Zimmermann B, Eckert E, Lassek E. Risk assessment of low-dose ethanol in food. *Food Chem Toxicol*. 2023;173:113633. doi:10.1016/j.fct.2023.113633
128. Yilmaz SGH, Goren AC. Halal Food and Metrology: ethyl Alcohol Contents of Beverages. *J Chem Metrol*. 2013;7(1):7–9.
129. Ali M, Batool S, Khalid N, et al. Alcoholic Off-Flavor Disorders in Fresh Fruits. *J Food Biochem*. 2023;2023:9–11. doi:10.1155/2023/3959653
130. Thewes FR, Brackmann A, Both V, et al. Dynamics of ethanol and its metabolites in fruit: the impact of the temperature and fruit species. *Postharvest Biol Technol*. 2023;197(November 2022):112209. doi:10.1016/j.postharvbio.2022.112209
131. Liu Z, Jiang F, Mo Y, Liao H, Chen P, Zhang H. Effects of Ethanol Treatment on Storage Quality and Antioxidant System of Postharvest Papaya. *Front Plant Sci*. 2022;13(June):1–11. doi:10.3389/fpls.2022.856499
132. Alsaleem T, Alsaleem T, Al-Dhelaan R, et al. Evaluation of Ethanol Formation in Fruit Juices During Refrigerated Storage Time and Its Halal Status. *Int J Halal Res*. 2022;4(1):19–28. doi:10.18517/ijhr.4.1.19-28.2022
133. Mishra K, Rathore M, Tickoo J, Kumar Singh A. Production of bioethanol from fruit waste. *Mater Today Proc*. 2022;68:1167–1171. doi:10.1016/j.matpr.2022.09.324
134. Casorso JG, Depasquale AN, Romero Morales S, et al. Seed dispersal syndrome predicts ethanol concentration of fruits in a tropical dry forest. *Proc R Soc B Biol Sci*. 2023;290(2003). doi:10.1098/rspb.2023.0804
135. Beaulieu M, Franke K, Fischer K. Feeding on ripening and over-ripening fruit: interactions between sugar, ethanol and polyphenol contents in a tropical butterfly. *J Exp Biol*. 2017;220(17):3127–3134. doi:10.1242/jeb.162008
136. Fine-Shamir N, Dahan A. Ethanol-based solubility-enabling oral drug formulation development: accounting for the solubility-permeability interplay. *Int J Pharm*. 2024;653(February):123893. doi:10.1016/j.ijpharm.2024.123893
137. Chung E, Reinaker K, Meyers R. Ethanol Content of Medications and Its Effect on Blood Alcohol Concentration in Pediatric Patients. *J Pediatr Pharmacol Ther*. 2024;29(2):188–194. doi:10.5863/1551-6776-29.2.188
138. Nayak BS, Mohanty B, Mishra B, Roy H, Nandi S. Transethosomes: cutting edge approach for drug permeation enhancement in transdermal drug delivery system. *Chem Biol Drug Des*. 2023;102(3):653–667. doi:10.1111/cbdd.14254
139. Emanet M, Ciofani G. Ethosomes as Promising Transdermal Delivery Systems of Natural-Derived Active Compounds. *Adv NanoBiomed Res*. 2023;3(10). doi:10.1002/anbr.202300020
140. Hmingthansanga V, Singh N, Banerjee S, Manickam S, Velayutham R, Natesan S. Improved Topical Drug Delivery: role of Permeation Enhancers and Advanced Approaches. *Pharmaceutics*. 2022;14(12). doi:10.3390/pharmaceutics14122818
141. Castangia I, Manconi M, Allaw M, et al. Mouthwash Formulation Co-Delivering Quercetin and Mint Oil in Liposomes Improved with Glycol and Ethanol and Tailored for Protecting and Tackling Oral Cavity. *Antioxidants*. 2022;11(2):1–12. doi:10.3390/antiox11020367
142. Jung YH, Heo DG, Lee DC, et al. Effect of concomitant oral administration of ethanol on the pharmacokinetics of nicardipine in rats. *Biomed Chromatogr*. 2022;36(9):e5425. doi:10.1002/bmc.5425
143. Srdjenovic B, Torovic L, Kladar N, Bozin B, Sudji J. Health risk assessment for pediatric population associated with ethanol and selected residual solvents in herbal based products. *Regul Toxicol Pharmacol*. 2019;107:104406. doi:10.1016/j.yrtph.2019.104406
144. Wang M, Yao PF, Sun PY, Liang W, Chen XJ. Key quality factors for Chinese herbal medicines entering the EU market. *Chin Med*. 2022;17(1):1–13. doi:10.1186/s13020-022-00583-x
145. Opuni KFM, Kretchy JP, Agyabeng K, et al. Contamination of herbal medicinal products in low-and-middle-income countries: a systematic review. *Heliyon*. 2023;9(9):e19370. doi:10.1016/j.heliyon.2023.e19370
146. Kelber O, Steinhoff B, Nauert C, et al. Ethanol in Herbal Medicinal Products for Children: no Toxicological Concerns. Pharm Ind. 2012;2012:1.
147. Vojvodić S, Čonić BS, Torović L. Safety assessment of herbal food supplements: ethanol and residual solvents associated risk. *J Food Compos Anal*. 2023;122:105483. doi:10.1016/j.jfca.2023.105483
148. Garcia-Parrilla MC, Torija MJ, Mas A, Cerezo AB, Troncoso AM. Chapter 25 - Vinegars and Other Fermented Condiments. In: Frias J, Martinez-Villaluenga C, editors. *Fermented Foods in Health and Disease Prevention*. Academic Press; 2017:577–591. doi:10.1016/B978-0-12-802309-9.00025-X
149. Ho CW, Lazim AM, Fazry S, Zaki UKHH, Lim SJ. Varieties, production, composition and health benefits of vinegars: a review. *Food Chem*. 2017;221:1621–1630. doi:10.1016/j.foodchem.2016.10.128
150. Kwon DY, Nyakudya E, Jeong YS. Fermentation: food Products. In: editor. *Encyclopedia of Agriculture and Food Systems*. Academic Press;2014:113–123. doi:10.1016/B978-0-444-52512-3.00155-8

151. Xia T, Zhang B, Duan W, Zhang J, Wang M. Nutrients and bioactive components from vinegar: a fermented and functional food. *J Funct Foods*. 2020;64(November 2019):103681. doi:10.1016/j.jff.2019.103681
152. Baharuddin AS, Amin NSM, Ruskam A, Yacob AR. Forensic determination of ethanol in import and local prepared vinegar for halal in accordance with Shafi'i school of jurisprudence. *Food Res*. 2022;6:1–9. doi:10.26656/FR.2017.6(S3).010
153. Pulungan I, Sugijanto K, Prawita A. Validation Gas Chromatography-Fid Method for Analysis of Ethanol Content in Vinegar Metode Validasi Gas Chromatography-Fid Untuk Analisis Konten Ethanol Pada Cuka. *J Halal Prod Res*. 2018;01(02):22–32.
154. Hamden Z, El-Ghoul Y, Alminderej FM, Saleh SM, Majdoub H. High-Quality Bioethanol and Vinegar Production from Saudi Arabia Dates: characterization and Evaluation of Their Value and Antioxidant Efficiency. *Antioxidants*. 2022;11(6). doi:10.3390/antiox11061155
155. Fisher JM, Wolever TMS, Campbell JE, Ezatagha A, Noronha JC, Jenkins AL. Effect of a Snack Bar Optimized to Reduce Alcohol Bioavailability: a Randomized Controlled Clinical Trial in Healthy Individuals. *J Med Food*. 2020;23(4):432–439. doi:10.1089/jmf.2019.0228
156. Younes S. The impact of micronutrients on the sense of taste. *Hum Nutr Metab*. 2024;35(December 2023):200231. doi:10.1016/j.hnm.2023.200231
157. Barnard ND. Micronutrients in Health and Disease. Available from: https://nutritionguide.pcrm.org/nutritionguide/view/Nutrition_Guide_for_Clinicians/1342057/all/Micronutrients_in_Health_and_Disease. Accessed November 6, 2020.
158. Pereira A, Adekunle RD, Zaman M, Wan MJ. Association Between Vitamin Deficiencies and Ophthalmological Conditions. *Clin Ophthalmol*. 2023;17(July):2045–2062. doi:10.2147/OPTH.S401262
159. Saha Turna N, Chung R, McIntyre L. A review of biogenic amines in fermented foods: occurrence and health effects. *Heliyon*. 2024;10(2):e24501. doi:10.1016/j.heliyon.2024.e24501
160. Simon Sarkadi L. Chapter 27 - Biogenic Amines in Fermented Foods and Health Implications. In: Frias J, Martinez-Villaluenga C, editors. *Fermented Foods in Health and Disease Prevention*. Academic Press; 2017:625–651. doi:10.1016/B978-0-12-802309-9.00027-3
161. Anderson LA. Herbal Supplements and Alcohol Interactions. 2017
162. Santy-Tomlinson J, Falaschi P, Hertz K *Interdisciplinary Nutritional Management and Care for Older Adults: an Evidence-Based Practical Guide for Nurses*.; 2021. doi:10.1007/978-3-030-63892-4_9.
163. Duniya Sheneni V, Eleojo Shaibu I. Drug interactions and drug-food interactions in patients receiving diabetes mellitus treatment. *Endocrinol Int J*. 2023;11(2):23–28. doi:10.15406/emij.2023.11.00327
164. Zacharia GS, Jacob A. Acetaminophen: a Liver Killer or Thriller. *Cureus*. 2023;15(10):e47071. doi:10.7759/cureus.47071
165. Care P, Alane T, Tor P, et al. Risky Alcohol Consumption in the Elderly: screening and Brief. *Beverages*. 2023;9(100):1–15.
166. Jochum C. Histamine Intolerance: symptoms, Diagnosis, and Beyond. *Nutrients*. 2024;16(8):1219. doi:10.3390/nu16081219
167. Seitz HK, Moreira B, Neuman MG. Pathogenesis of Alcoholic Fatty Liver a Narrative Review. *Life*. 2023;13(8):1–17. doi:10.3390/life13081662
168. Rabelo ACS, de L Andrade AKDL, Costa DC. The Role of Oxidative Stress in Alcoholic Fatty Liver Disease: a Systematic Review and Meta-Analysis of Preclinical Studies. *Nutrients*. 2024;16(8):1174. doi:10.3390/nu16081174
169. Nor NF, Ahmad H, Ariffin AS. Potencies and Opportunities of Halal Market in Global Industry: an Empirical Analysis of Malaysia and Indonesia. *HALAL REVIEWS*. 2023;3(1):1–24. doi:10.55265/halalreviews.v3i1.14
170. Herdiana Y, Sofian FF, Shamsuddin S, Rusdiana T. Towards halal pharmaceutical: exploring alternatives to animal-based ingredients. *Heliyon*. 2024;10(1):e23624. doi:10.1016/j.heliyon.2023.e23624
171. Abdallah A, Rahem MA, Pasqualone A. The multiplicity of halal standards: a case study of application to slaughterhouses. *J Ethn Foods*. 2021;8(1):1. doi:10.1186/s42779-021-00084-6
172. Liu B-X, Yang J, Zeng C, Dai X-J, Chen Y. Risk of inflammatory bowel disease appears to vary across different frequency, amount, and subtype of alcoholic beverages. *Front Nutr*. 2022;9. doi:10.3389/fnut.2022.918754
173. Osaki A, Okazaki Y, Kimoto A, Izu H, Kato N. Beneficial effect of a low dose of ethanol on liver function and serum urate in rats fed a high-fat diet. *J Nutr Sci Vitaminol*. 2014;60(6):408–412. doi:10.3177/jnsv.60.408
174. Diao Y, Nie J, Tan P, et al. Long-term low-dose ethanol intake improves healthspan and resists high-fat diet-induced obesity in mice. *Aging*. 2020;12(13):13128–13146. doi:10.18632/aging.103401
175. Gauthier TW, du Ping X, Harris FL, Brown LAS. Liposomal Glutathione Augments Immune Defenses against Respiratory Syncytial Virus in Neonatal Mice Exposed in Utero to Ethanol. *Antioxidants*. 2024;13(137):1–18.