TẠP CHÍ KHOA HỌC & CÔNG NGHỆ ĐẠI HỌC DUY TÂN
DTU Journal of Science and Technology 5(60) (2023) 102-113

TRƯỜNG ĐẠI HỌC DUY TÂN
DUYTAN UNIVERSITY

Metabolism and harmful effects of alcohol on health

Cơ chế chuyển hóa và những tác hại của rượu đối với sức khỏe

Nguyen Minh Hung
Nguyễn Minh Hùng

Center for Pharmaceutical Biotechnology, College of Medicine and Pharmacy, Duy Tan University, 550000, Da Nang, Vietnam
Trung tâm Công nghệ Sinh học Dược, Trường Y Dược, Đại học Duy Tân, Đà Nẵng, Việt Nam

(Ngày nhận bài: 17/8/2023, ngày phản biện xong: 12/9/2023, ngày chấp nhận đăng: 20/10/2023)

Abstract

The present review paper provides a comprehensive examination of alcohol consumption, focusing on its metabolism and health effects. Alcohol, a substance that depresses the central nervous system (CNS), is widely consumed and holds significant social and cultural significance. Understanding the metabolism of alcohol is vital for comprehending its effects on the human body and the factors influencing alcohol-induced health outcomes. This review aims to synthesize existing literature to shed light on the intricate interplay between alcohol consumption, metabolism, and health outcomes.

Keywords: ADH; alcohol consumption; alcohol dehydrogenase; aldehyde dehydrogenase; ALDH; health effects.

Tóm tắt

Bài báo này trình bày một cách toàn diện về việc tiêu thụ rượu, cơ chế chuyển hóa và tác hại của nó đối với sức khỏe. Rượu là một hợp chất ức chế thần kinh trung ương được sử dụng rộng rãi và có ý nghĩa đối với văn hóa và xã hội. Hiểu được quá trình chuyển hóa rượu sẽ nâng cao nhận thức về những tác tại của rượu đối với sức khỏe con người. Bài tổng quan này nhằm mục đích làm sáng tỏ mối tương tác phức tạp giữa việc uống rượu, quá trình trao đổi chất và những tác hại đến sức khỏe con người.

Từ khóa: ADH; sử dụng rượu; alcohol dehydrogenase; aldehyde dehydrogenase; ALDH; ảnh hưởng của rượu.

1. Introduction

Alcohol consumption has an extensive historical and cultural heritage, spanning millennia. It has played an integral role in various social, religious, and ceremonial practices across diverse societies, with its significance varying among different cultures. The recreational use of alcohol has been deeply rooted in human civilization, and persisting into modern era. Throughout history, alcohol has featured prominently in social functions, such as celebrations, gatherings, and fostering social bonds. It has also been a central element in rituals, rites of passage, and traditional customs, serving as a vital component of cultural identity in numerous regions worldwide. Moreover, alcohol beverages have been employed for medicinal purposes for centuries, with

*Corresponding Author: Nguyen Minh Hung
Email: hungmolbio@gmail.com

traditional remedies often relying on their alleged healing properties [1].

However, the widespread consumption of alcohol also presents significant challenges and concerns. Its recreational use carries the potential to lead to various adverse consequences, impacting both individuals and societies at large. Excessive alcohol consumption stands as a major risk factor for a wide spectrum of health issues, including liver diseases, cardiovascular disorders, mental health ailments, and an increased susceptibility to accidents and injuries [2]. The economic ramifications of alcohol misuse are substantial, imposing burdens on healthcare systems, productivity losses, as well as the expenses associated with law enforcement and rehabilitation programs [3]. Furthermore, the presence of alcohol use disorder (AUD) and alcohol addiction poses serious public health challenges [4], affecting millions of individuals worldwide and imposing substantial emotional and financial burdens on those affected, their families, and communities [5]. This review paper seeks to consolidate existing research to provide a comprehensive understanding of alcohol metabolism and its effects on health. By shedding light on these aspects, this review aims to contribute to ongoing efforts to address alcohol-related issues and promote responsible alcohol consumption for the benefit of individual and public health.

2. Alcohol metabolism

2.1. Overview of alcohol metabolism pathway

Alcohol metabolism is a multifaceted process primarily centered in the liver [6], although other organs, such as the brain and gastrointestinal tract, play secondary roles [6]. This metabolic pathway involves a series of enzymatic reactions that convert ethanol, the active component in alcoholic beverages, into less harmful compounds for eventual elimination from the body [7]. The principal enzymes involved in alcohol metabolism are alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) [7]. These enzymes are distributed throughout various tissues, cooperating to convert ethanol into acetaldehyde and subsequently into acetate [7]. The breakdown of alcohol occurs in two main steps:

Step 1: ADH Reaction: In this initial phase of alcohol metabolism, the enzyme ADH catalyzes the conversion of ethanol into acetaldehyde. ADH achieves this by extracting two hydrogen atoms from ethanol, concurrently converting NAD^+ into NADH [7]. The reaction can be represented as follows:

$$\text{Ethanol} + NAD^+ \rightarrow \text{Acetaldehyde} + NADH + H^+$$

The formation of acetaldehyde is crucial because it is a toxic substance, potentially causing cellular damage and various health issues if its concentration rises excessively [8, 9].

Step 2: ALDH Reaction: The second stage involves the enzyme ALDH, further metabolizing acetaldehyde into acetate. ALDH facilitates this process by catalyzing the oxidation of acetaldehyde and adding a water molecule, resulting in the formation of acetate [7]. The reaction can be represented as follows:

$$\text{Acetaldehyde} + NAD^+ + H_2O \rightarrow \text{Acetate} + NADH + H^+$$

Acetate, the final product of alcohol metabolism, is a relatively harmless substance [10] and can be subsequently metabolized into carbon dioxide and water for elimination from the body [10] or utilized as an energy source [10].

Individuals may exhibit diverse rates of alcohol metabolism influenced by genetic factors [11]. Genetic variations in the genes encoding ADH and ALDH enzymes can impact the efficiency of ethanol metabolism [11]. For

example, some individuals possess specific ADH and ALDH variants, such as *ADH1B* and *ADH1C* alleles, resulting in accelerated alcohol metabolism and reduced susceptibility to alcohol-related health problems [11]. Conversely, individuals with particular genetic variants, such as *ALDH2* allele, may experience slower alcohol metabolism, increasing their susceptibility to alcohol-related disorders. While the liver is the primary organ responsible for alcohol metabolism, other organs contribute a minor extent. The brain and gastrointestinal tract contain limited ADH enzymes, contributing to a small amount of alcohol metabolism when compared to the liver [12].

Overall, ADH and ALDH enzymes are pivotal in alcohol metabolism, converting ethanol into acetaldehyde and further into acetate. Genetic variations in these enzymes can influence an individual's rate of alcohol metabolism and tolerance, thereby impacting their susceptibility to alcohol-related health conditions. Understanding the roles of ADH and ALDH is essential for comprehending alcohol metabolism and its implications for both individual health and public health strategies.

2.2. Factors influencing alcohol metabolism

Alcohol metabolism is a complex process influenced by various factors, including genetics, gender, age, and other individual characteristics [6]. An in-depth understanding of these factors is essential, as they play a significant role in determining an individual's alcohol tolerance, susceptibility to alcohol-related health concerns, and potential risk of developing AUD. Here, we delve into the key factors that influence alcohol metabolism. *Genetic variations*: Genetic factors play a pivotal role in alcohol metabolism, giving rise to individual disparities in alcohol tolerance and responsiveness. Variations within the genes responsible for encoding ADH and ALDH enzymes, as mentioned earlier, can dramatically affect the pace of alcohol breakdown. For example, some individuals may carry specific ADH and ALDH gene variants that foster more efficient alcohol metabolism, resulting in the rapid conversion of ethanol into less harmful substances. Consequently, such individuals often exhibit higher alcohol tolerance and a reduced susceptibility to adverse alcohol effects like facial flushing and nausea. Conversely, others may bear genetic variants of ADH and ALDH linked to slower alcohol metabolism, leading to acetaldehyde accumulation and adverse reactions, even with modest alcohol consumption. This genetic predisposition is notably prominent in certain East Asian populations, contributing to lower alcohol consumption rates in these groups [13]; *Gender*: Gender disparities exert a notable impact on alcohol metabolism. In general, women tend to metabolize alcohol at a slower rate than men, primarily due to physiological differences. Women typically possess a higher proportion of body fat and a lower proportion of water compared to men with similar weight. As alcohol is water-soluble and does not accumulate in fatty tissues, women often experience higher blood alcohol concentrations when consuming equivalent amounts of alcohol. Additionally, women typically have lower levels of ADH enzymes, further contributing to a decelerated alcohol metabolism [14]; *Age*: Age is a substantial determinant of alcohol metabolism. Generally, alcohol metabolism becomes less efficient as individuals age. This phenomenon is partially attributed to the diminishing functionality of the liver and shifts in enzyme activity over time. With advancing age, the liver's ability to metabolize alcohol declines, resulting in prolonged alcohol effects on the body.

Moreover, older individuals may exhibit increased sensitivity to alcohol, necessitating smaller quantities to attain comparable effects relative to their younger counterparts [15]; *Liver Health*: The liver plays a central role in alcohol metabolism. Conditions affecting liver health, such as liver diseases or damage caused by chronic alcohol consumption, can significantly impede alcohol metabolism. In cases of liver impairment, the effectiveness of ADH and ALDH enzymes may diminish, extending exposure to acetaldehyde and its adverse effects on the body; *Medications and Drug Interactions*: certain medications can interact with alcohol metabolism, either by inhibiting ADH and ALDH enzymes or by affecting liver function [16]. For example, medications that inhibit ADH and ALDH can slow down alcohol metabolism and increase the risk of acetaldehyde accumulation, resulting in adverse reactions to alcohol [17]. Furthermore, some drugs may exacerbate the toxic effects of alcohol on the liver, potentially leading to severe liver damage [16]; *Ethnicity and Race*: ethnicity and race can also influence alcohol metabolism. As mentioned earlier, some East Asian populations have a higher prevalence of genetic variants that lead to slower alcohol metabolism, making them more susceptible to acetaldehyde accumulation and its associated adverse reactions.

In summary, alcohol metabolism is influenced by various factors, including genetic variations in ADH and ALDH enzymes, gender, age, liver health, medications, and ethnicity. These factors collectively contribute to individual differences in alcohol tolerance and response, as well as the risk of developing alcohol-related health issues. Understanding these influences is essential for promoting responsible alcohol consumption and tailoring prevention and treatment strategies for alcohol-related disorders.

2.3. Alcohol metabolism in different organs

Alcohol metabolism predominantly takes place in the liver, where the primary enzymatic reactions occur. Nevertheless, various other organs, such as the brain, gastrointestinal tract, and lungs, also play a role in alcohol metabolism to a lesser degree. Here, we discuss alcohol metabolism in different organs. *Brain*: while the brain primarily acts as a target for the effects of alcohol rather than a site of metabolism, it does play a minor role in alcohol metabolism [18]. The brain contains some ADH enzymes, although in smaller quantities compared to the liver [19]. These enzymes participate in the breakdown of ethanol into acetaldehyde within the brain tissue itself. Notably, acetaldehyde can exert various effects on the brain, including impairing cognitive functions and influencing neurotransmitter activity [20]. Furthermore, acetaldehyde is involved in the formation of harmful byproducts known as free radicals, which can contribute to oxidative stress and brain damage in chronic alcohol users [21, 22]; *Gastrointestinal tract*: the gastrointestinal (GI) tract also contributes minimally to alcohol metabolism [23]. Some ADH enzymes are present in the mucosal lining of the GI tract, particularly in the stomach. These enzymes metabolize a small portion of ingested alcohol before it reaches the liver. However, the alcohol metabolized in the GI tract is only a small amount of the total alcohol consumed [23]. The majority of alcohol metabolism occurs in the liver after it is absorbed into the bloodstream; *Lungs*: a small fraction of alcohol can be eliminated from the body unchanged through the lungs [24]. This is the reason why individuals who consume alcohol may have detectable amounts of alcohol in their breath, which is the principle behind breathalyzer tests used to measure blood alcohol concentration (BAC) for legal purposes. The elimination of

alcohol through the lungs is minimal and generally not significant compared to the metabolism that occurs in the liver [24].

It is noteworthy that the efficiency of alcohol metabolism in different organs can be influenced by various factors, including genetics, liver health, gender, and the presence of other substances in the body. Chronic and excessive alcohol consumption can overload the liver's capacity to metabolize alcohol, leading to systemic effects on other organs, including the brain and the gastrointestinal tract. Moreover, the presence of certain medications or medical conditions can also interact with alcohol metabolism and alter its effects on different organs.

3. Health effects of alcohol consumption

3.1. Long-term effects on the liver

Alcoholic liver disease (ALD) is a serious and potentially life-threatening condition caused by chronic and excessive alcohol consumption over an extended period. The liver is the primary organ responsible for metabolizing alcohol, and prolonged alcohol abuse can lead to various forms of liver damage. ALD encompasses a spectrum of liver disorders, ranging from early-stage fatty liver to more severe conditions like alcoholic hepatitis and cirrhosis. Here are the key aspects of ALD and its long-term effects on the liver. *Fatty liver* (steatosis): fatty liver, or steatosis, is the earliest and most prevalent form of ALD. It occurs when fat accumulates in liver cells due to excessive alcohol consumption [25]. Fatty liver is usually asymptomatic and reversible if alcohol consumption is ceased at this stage [25]. However, continued heavy drinking can progress the condition into more severe forms of ALD [25]; *Alcoholic hepatitis*: alcoholic hepatitis is a more advanced stage of ALD characterized by inflammation and damage to liver cells. It typically occurs in individuals with a history of chronic alcohol abuse. Symptoms may include jaundice (yellowing of the skin and eyes), abdominal pain, fever, and liver enlargement. Alcoholic hepatitis is potentially life-threatening, and prompt medical intervention is necessary to prevent further progression [26]; *Alcoholic cirrhosis*: cirrhosis is the most severe form of ALD and is characterized by extensive scarring (fibrosis) of liver tissue. The scar tissue replaces healthy liver cells, impairing liver function. Alcoholic cirrhosis is irreversible and can lead to liver failure. Common symptoms include fluid retention (edema), ascites (abdominal fluid buildup), and a significant decline in liver function [25]; *Fibrosis and NASH*: in addition to alcoholic cirrhosis, long-term alcohol abuse can lead to liver fibrosis, which is the buildup of scar tissue in the liver. Fibrosis is an intermediate stage between fatty liver and cirrhosis. Nonalcoholic steatohepatitis (NASH), which resembles alcoholic hepatitis but occurs in individuals who do not consume alcohol, can also be caused by chronic alcohol consumption; *Liver cancer*: prolonged alcohol abuse increases the risk of developing liver cancer, also known as hepatocellular carcinoma (HCC). Chronic inflammation and liver damage resulting from ALD contribute to the development of cancerous cells within the liver. Liver cancer is a serious condition with a poor prognosis, and can develop at any stage of ALD [25]; *Impact on liver function*: ALD significantly impairs liver function. The liver plays a crucial role in metabolizing toxins, processing nutrients, and producing essential proteins. With ALD, these functions are compromised, leading to a range of health issues such as malnutrition, blood clotting abnormalities, and an increased susceptibility to infections [27]; *Factors affecting ALD severity*: the severity of ALD can vary among individuals based on various factors, including

genetics, overall health, and the duration and amount of alcohol consumption. Some individuals may develop ALD even with relatively lower levels of alcohol consumption, while others may consume higher amounts without experiencing severe liver damage. Genetic factors, including variations in the ADH and ALDH enzymes previously mentioned, also influence an individual's susceptibility to ALD [28].

Prevention and Treatment: The most effective way to prevent ALD is to either limit alcohol consumption to moderate levels or abstain from alcohol entirely. For individuals already diagnosed with ALD, the primary treatment involves complete abstinence from alcohol to halt the progression of liver damage. Medical interventions, lifestyle changes, and nutritional support may also be prescribed to manage ALD and its associated complications.

In conclusion, alcoholic liver disease is a range of liver disorders caused by chronic and excessive alcohol consumption. It includes fatty liver, alcoholic hepatitis, alcoholic cirrhosis, fibrosis, and an increased risk of liver cancer. ALD can lead to severe liver damage and life-threatening complications. Early recognition, prompt intervention, and the cessation of alcohol consumption are crucial for managing ALD and improving liver health.

3.2. Cardiovascular effects

While moderate alcohol consumption has been associated with potential cardiovascular benefits [29], excessive and chronic alcohol use can have detrimental effects on the cardiovascular system. The relationship between alcohol consumption and cardiovascular health is complex and can vary based on factors such as the amount of alcohol consumed, individual characteristics, and overall lifestyle [29]. Here, we highlight the key cardiovascular effects associated with alcohol consumption. *Cardiovascular benefits of moderate alcohol consumption*: moderate alcohol intake, typically defined as up to one drink per day for women and up to two drinks per day for men, has been associated with potential cardiovascular benefits [29]. Some studies suggest that moderate alcohol intake may confer a protective effect against certain cardiovascular conditions, such as coronary artery disease (CAD) and ischemic stroke [30]. It is believed that alcohol's potential benefits on cardiovascular health may be due to its ability to increase high-density lipoprotein (HDL) cholesterol levels, often referred to as "good cholesterol," and reduce the risk of blood clot formation [31]; *Increased risk of high blood pressure* (hypertension): chronic and heavy alcohol consumption is a well-established risk factor for hypertension, commonly known as high blood pressure. Alcohol can lead to an increase in blood pressure levels, especially when consumed in large quantities. High blood pressure is a significant risk factor for various cardiovascular diseases, including heart attack, stroke, and heart failure [32]; *Cardiomyopathy*: prolonged and heavy alcohol usage can result in a condition known as alcoholic cardiomyopathy. This condition is characterized by weakened heart muscles, leading to reduced pumping efficiency and an enlarged heart. Alcoholic cardiomyopathy can result in heart failure, where the heart fails to pump enough blood to meet the body's needs [33]; *Irregular heartbeat* (Arrhythmias): alcohol consumption can trigger or exacerbate certain cardiac arrhythmias, characterized by irregular heart rhythms. A notable example is atrial fibrillation (AFib), wherein the heart's upper chambers quiver instead of beating regularly. AFib can lead to blood clots, stroke, and other complications [34]; *Increased risk of stroke*: while moderate alcohol consumption may be associated with a lower risk of ischemic

stroke, excessive alcohol consumption can increase the risk of both ischemic and hemorrhagic strokes. Hemorrhagic strokes occur when a blood vessel in the brain ruptures, causing bleeding into the brain tissue. Alcohol's effect on blood clotting and blood vessel integrity can contribute to this increased risk [34]; *Impact on blood lipids*: excessive alcohol consumption can negatively impact blood lipid profiles, leading to higher levels of triglycerides and low-density lipoprotein (LDL) cholesterol, often referred to as "bad cholesterol". Elevated levels of these lipids are associated with an increased risk of atherosclerosis, the buildup of fatty deposits in the arteries that can lead to CAD [31]; *Dilated cardiomyopathy*: another form of cardiomyopathy associated with alcohol abuse is dilated cardiomyopathy. In this condition, the heart chambers become enlarged and weakened, reducing the heart's ability to pump blood effectively [33]; *Increased risk of sudden cardiac death*: excessive alcohol consumption has been linked to an increased risk of sudden cardiac death. This is a sudden, unexpected loss of heart function, typically due to an electrical problem in the heart's rhythm [31].

It is important to emphasize that any potential cardiovascular benefits from alcohol consumption are outweighed by the risks associated with excessive alcohol use. The American Heart Association advises that individuals who do not currently drink alcohol should not start for potential heart health benefits. For those who do consume alcohol, moderation is essential to reduce the risk of alcohol-related cardiovascular complications. It is crucial to consult with a healthcare provider to assess individual risk factors and make informed decisions regarding alcohol consumption and cardiovascular health. Additionally, lifestyle factors such as a balanced diet, regular exercise, and not smoking play a more significant role in promoting heart health than alcohol consumption alone.

3.3. Effects on mental health

Alcohol's impact on mental health is profound, influencing mood, cognitive abilities, and the course of existing mental health conditions. While some may initially experience fleeting mood elevation from alcohol, extended and excessive use precipitates detrimental mental health outcomes. Here are the primary ways in which alcohol affects mental well-being. *Depression and anxiety:* as a central nervous system depressant, alcohol's excessive consumption amplifies depression and anxiety symptoms. While offering temporary respite from negativity, it can exacerbate underlying issues, creating a cycle of alcohol dependency to manage distress, further intensifying depression and anxiety. *Suicidal ideation and self-harm:* alcohol and suicidal tendencies are intertwined, with complex interplays. Factors such as pre-existing mental health conditions and social elements contribute. Alcohol impairs judgment, fostering impulsivity that heightens the risk of self-harm and suicide [35]. *Cognitive impairment and memory reduction:* alcohol significantly impairs cognitive function and memory, both in the short term and over extended periods. Excessive alcohol consumption can result in memory blackouts during periods of intoxication, while chronic abuse can lead to persistent cognitive deficits that affect learning, memory, and attention. These impairments significantly diminish the quality of daily life [36]. *Insomnia and sleep disruptions:* while alcohol initially induces drowsiness, it ultimately disrupts the sleep cycle, leading to a deterioration in sleep quality. This disruption, particularly in rapid eye movement (REM) sleep, which is crucial for restoration and emotional balance, can contribute to mood disorders and exacerbate

existing mental health conditions [37]. *Aggression and impulsive conduct:* Alcohol's inhibition reduction can spur aggression and impulsivity, fostering violence and recklessness. "Disinhibition" triggers risky behaviors with potential legal and social ramifications. *Psychosis and hallucinations:* Alcohol excess can evoke alcohol-induced psychosis, marked by hallucinations, delusions, and confused thoughts. These manifestations arise during heavy drinking or withdrawal.

Chronic and excessive alcohol use culminates in Alcohol Use Disorder (AUD), characterized by uncontrollable alcohol intake, preoccupation with alcohol, and continued use despite negative consequences. AUD can give rise to a range of mental health issues, significantly impacting overall well-being and functionality. Importantly, the interaction between alcohol and mental health varies based on genetics, personal mental health history, and an individual's resilience. While some people may experience worsened mental health, others may remain more resilient. However, chronic heavy alcohol use generally heightens the risk of mental health issues and exacerbates pre-existing conditions. For individuals with a history of mental health concerns, caution in alcohol consumption is paramount. Seeking guidance from healthcare professionals is advisable if there are concerns about the mental health effects of alcohol. Seeking assistance for alcohol-related problems and addressing mental health challenges is pivotal for improved mental well-being.

3.4. Impact on gastrointestinal health

Alcohol consumption can have significant detrimental effects on the gastrointestinal (GI) tract, ranging from acute irritations to chronic conditions. Alcohol has the potential to irritate the sensitive lining of the digestive system, leading to various GI issues. Here are the key impacts of alcohol on gastrointestinal health. *Gastritis*: gastritis is characterized by inflammation of the stomach lining. Excessive alcohol consumption can irritate and inflame the stomach mucosa, resulting in acute gastritis. Symptoms of gastritis may include abdominal pain, nausea, vomiting, and a sensation of fullness. Chronic alcohol abuse can lead to persistent gastritis, increasing the risk of more severe complications; *Peptic ulcers*: alcohol use can exacerbate or contribute to the development of peptic ulcers, which are sores that form on the lining of the stomach, small intestine, or esophagus. Alcohol irritates and weakens the protective lining of the digestive tract, making it more susceptible to damage from stomach acids. Individuals with existing ulcers are advised to avoid alcohol, as it can exacerbate the condition and delay the healing process; *Gastroesophageal reflux disease* (GERD): GERD is a chronic condition characterized by the backflow of stomach acid into the esophagus, resulting in heartburn and irritation. Alcohol can relax the lower esophageal sphincter (LES), a muscular ring that separates the esophagus from the stomach. A relaxed LES permits stomach acid to flow back into the esophagus, leading to GERD symptoms [38]; *Pancreatitis*: pancreatitis is the inflammation of the pancreas, a gland responsible for producing digestive enzymes and insulin. Chronic alcohol use is a common cause of pancreatitis, as alcohol irritates the pancreas and can trigger inflammation. Acute pancreatitis is a severe condition that requires immediate medical attention [39]; *Alcoholic fatty liver*: in addition to its impact on the liver (as discussed in section 3.2), alcohol can lead to the development of alcoholic fatty liver, a condition characterized by the accumulation of fat in liver cells. Fatty liver can contribute to liver inflammation and compromise liver function; *Malabsorption of nutrients*: alcohol

can impair the absorption of essential nutrients in the GI tract. Chronic alcohol consumption can result in malabsorption of vitamins (e.g., vitamin B12, folate) and minerals (e.g., calcium, magnesium), potentially causing deficiencies with various health consequences [40]; *Increased risk of GI cancers*: prolonged and heavy alcohol use has been associated with an increased risk of developing various GI cancers, including esophageal, stomach, and colorectal cancers. Chronic alcohol consumption can damage the cells lining the digestive tract, increasing the likelihood of cancer development [40]; *Diarrhea and irritable bowel syndrome* (IBS): alcohol consumption can irritate the intestines, leading to diarrhea and exacerbating symptoms of irritable bowel syndrome (IBS) in susceptible individuals. Individuals with a history of GI issues should be cautious about alcohol consumption, as it can worsen existing conditions and lead to new GI problems. Additionally, individuals experiencing acute GI symptoms after alcohol consumption should promptly seek medical attention.

The adverse effects of alcohol on gastrointestinal health underscore the importance of responsible alcohol consumption and being mindful of individual tolerance levels. Moderating alcohol intake and seeking medical advice for individuals with pre-existing GI conditions are essential steps to minimize the risk of alcohol-related GI issues.

3.5. Influence on reproductive health

The profound impact of alcohol on reproductive health has far-reaching consequences, affecting fertility, pregnancy outcomes, and the overall well-being of both mothers and infants. The intricate relationship between alcohol and reproduction underscores several pivotal facets worth understanding.

The delicate balance of reproductive hormones, so crucial in orchestrating the processes of conception, is susceptible to disruption from excessive alcohol consumption, affecting both men and women [41]. In men, this can lead to reduced testosterone levels, compromised sperm production, and irregular sperm morphology [41]. Women who engage in heavy alcohol use may experience disruptions in their menstrual cycles, resulting in irregular periods and anovulation, which is the absence of ovulation [41]. These hormonal fluctuations collectively contribute to fertility challenges, making conception a more difficult endeavor [41]. Alcohol's impact extends further to include infertility, affecting both genders [41]. In women, this arises from alcohol-induced hormonal imbalances and disruptions in ovulation, making it more difficult to conceive. In men, alcohol-related sperm irregularities hinder fertility and prolong the time it takes to conceive [46]. The presence of alcohol in pregnancy scenarios poses significant risks and can lead to a range of complications known as fetal alcohol spectrum disorders (FASDs) [41]. These complexities encompass various physical, behavioral, and cognitive disabilities in newborns. Fetal alcohol syndrome (FAS), characterized by distinctive facial features, developmental delays, and central nervous system anomalies, is one of the most severe outcomes of prenatal alcohol exposure [41]. The link between alcohol and miscarriage is evident, as alcohol consumption during pregnancy increases the risk of miscarriage, which involves the abrupt loss of pregnancy before the 20-week mark [41]. The precarious association between alcohol and preterm births, as well as reduced birth weights, adds to the seriousness of the situation [42]. Pregnant women affected by alcohol are at a higher risk of delivering prematurely (before 37 weeks of gestation) and having underweight infants,

leading to a cascade of health complications and developmental setbacks [42]. Neonatal abstinence syndrome (NAS) is a poignant manifestation, resulting from prenatal alcohol exposure that causes withdrawal symptoms in newborns, including irritability, tremors, feeding difficulties, and other issues [43]. Even breastfeeding is not immune to the challenges posed by alcohol, as its consumption by nursing mothers can infiltrate breast milk [41]. While occasional, moderate alcohol consumption may have minimal impact on breastfed infants, excessive and frequent indulgence can affect infant sleep patterns, motor development, and overall well-being [41].

It is crucially important for individuals who are planning to conceive or are already pregnant to abstain from alcohol to optimize maternal and neonatal outcomes. For those dealing with alcohol use disorder (AUD) and aspiring to become parents, seeking professional therapeutic intervention is essential to address alcohol dependence before conception.

In summary, the harmful connection between alcohol and reproductive health disrupts hormonal balance, increases infertility risks, and leads to adverse pregnancy outcomes, including FASDs, miscarriage, preterm birth, and low birth weight. While challenging, abstaining from alcohol during pregnancy and conception is the cornerstone for ensuring the overall well-being of both mother and child.

3.6. The association between alcohol consumption and cancer

The undeniable connection between alcohol consumption and cancer is firmly grounded in extensive research, consistently unveiling a clear and concerning correlation. The International Agency for Research on Cancer (IARC) has classified alcohol as a Group 1 carcinogen, leaving a room for doubt regarding its unequivocal carcinogenicity to humans [42]. The interplay between alcohol intake and cancer involves several crucial aspects:

Increased cancer risk: Excessive alcohol consumption is closely associated with an elevated risk of cancer types. Among the most prominent are head and neck cancers, which encompass conditions affecting the oral cavity, throat, voice box, and esophagus. Notably, the risk escalates significantly when heavy alcohol consumption is combined with tobacco use [42]. Alcohol's culpability extends to breast cancer, where even modest levels of consumption are linked to an increased risk. Importantly, the risk rises as alcohol intake increases, establishing a linear relationship between consumption and risk [48]. In the realm of cancer, liver cancer is a significant concern associated with chronic alcohol use. Alcohol-induced liver cirrhosis and subsequent damage markedly elevate the likelihood of hepatocellular carcinoma, the predominant form of liver cancer [44]. Alcohol’s influence also extends to colorectal cancer, attributed to its role in promoting chronic inflammation within the digestive tract. This persistent inflammation becomes a fertile ground for the development of cancer, reinforcing the connection [44]. Alcohol emerges as a risk factor for pancreatic cancer, a particularly deadly form with a dismal survival rate [45].

In summary, the undeniable link between alcohol and cancer is further underscored by its classification as a Group 1 carcinogen. Its intricate involvement in various cancers such as head and neck cancers, rreast cancer, liver cancer, colorectal cancer, and pancreatic cancer emphasizes the important of heightened awareness and responsible moderation to mitigate these formidable risks.

4. Conclusion

In conclusion, the review paper on alcohol consumption provides a comprehensive

analysis covering various aspects related to alcohol metabolism and health effects. The key findings include insights into alcohol metabolism pathways, factors influencing alcohol metabolism, and long-term health consequences.

References

[1] Mandelbaum DG. (1965). Alcohol and Culture. *Current Anthropology*, *6*, 281-293.

[2] Rehm J. (2011). The risks associated with alcohol use and alcoholism. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *34*, 135-143.

[3] Burke TR. (1988). The economic impact of alcohol abuse and alcoholism. *Public health reports (Washington, DC : 1974)*, *103*, 564-568.

[4] Finn SW, Mejldal A, Nielsen AS. (2023). Public stigma and treatment preferences for alcohol use disorders. *BMC health services research*, *23*, 76. DOI:10.1186/s12913-023-09037-y

[5] Ramkissoon R, Shah VH. (2022). Alcohol Use Disorder and Alcohol-Associated Liver Disease. *Alcohol research : current reviews*, *42*, 13. DOI:10.35946/arcr.v42.1.13

[6] Cederbaum AI. (2012). Alcohol metabolism. *Clinics in liver disease*, *16*, 667-685. DOI:10.1016/j.cld.2012.08.002

[7] Jiang Y, Zhang T, Kusumanchi P, *et al.* (2020). Alcohol Metabolizing Enzymes, Microsomal Ethanol Oxidizing System, Cytochrome P450 2E1, Catalase, and Aldehyde Dehydrogenase in Alcohol-Associated Liver Disease. *Biomedicines*, *8*. DOI:10.3390/biomedicines8030050

[8] Beauchamp RO, Jr., St Clair MB, Fennell TR, *et al.* (1992). A critical review of the toxicology of glutaraldehyde. *Critical reviews in toxicology*, *22*, 143-174. DOI:10.3109/10408449209145322

[9] Mizumoto A, Ohashi S, Hirohashi K, *et al.* (2017). Molecular Mechanisms of Acetaldehyde-Mediated Carcinogenesis in Squamous Epithelium. *Int J Mol Sci*, *18*. DOI:10.3390/ijms18091943

[10] Zakhari S. (2006). Overview: how is alcohol metabolized by the body? *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *29*, 245-254.

[11] Edenberg HJ. (2007). The genetics of alcohol metabolism: role of alcohol dehydrogenase and aldehyde dehydrogenase variants. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *30*, 5-13.

[12] Haseba T, Ohno Y. (2010). A new view of alcohol metabolism and alcoholism--role of the high-Km Class III alcohol dehydrogenase (ADH3). *International journal of environmental research and public health*, *7*, 1076-1092. DOI:10.3390/ijerph7031076

[13] Wall TL, Ehlers CL. (1995). Genetic Influences Affecting Alcohol Use Among Asians. *Alcohol health and research world*, *19*, 184-189.

[14] Mumenthaler MS, Taylor JL, O'Hara R, *et al.* (1999). Gender differences in moderate drinking effects. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *23*, 55-64.

[15] Meier P, Seitz HK. (2008). Age, alcohol metabolism and liver disease. *Current opinion in clinical nutrition and metabolic care*, *11*, 21-26. DOI:10.1097/MCO.0b013e3282f30564

[16] Weathermon R, Crabb DW. (1999). Alcohol and medication interactions. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *23*, 40-54.

[17] Lai CL, Li YP, Liu CM, *et al.* (2013). Inhibition of human alcohol and aldehyde dehydrogenases by cimetidine and assessment of its effects on ethanol metabolism. *Chemico-biological interactions*, *202*, 275-282. DOI:10.1016/j.cbi.2012.11.016

[18] Spanagel R, Zink M, Sommer WH, *Neurobiology of Alcohol Addiction*, in *Neuroscience in the 21st Century: From Basic to Clinical*, D.W. Pfaff, Editor. 2013, Springer New York: New York, NY. p. 2745-2773.

[19] Heit C, Dong H, Chen Y, *et al.* (2013). The role of CYP2E1 in alcohol metabolism and sensitivity in the central nervous system. *Sub-cellular biochemistry*, *67*, 235-247. DOI:10.1007/978-94-007-5881-0_8

[20] Quertemont E, Didone V. (2006). Role of acetaldehyde in mediating the pharmacological and behavioral effects of alcohol. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *29*, 258-265.

[21] Wu D, Cederbaum AI. (2003). Alcohol, oxidative stress, and free radical damage. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *27*, 277-284.

[22] Weil ZM, Corrigan JD, Karelina K. (2018). Alcohol Use Disorder and Traumatic Brain Injury. *Alcohol research : current reviews*, *39*, 171-180.

[23] Pronko P, Bardina L, Satanovskaya V, *et al.* (2002). Effect of chronic alcohol consumption on the ethanol- and acetaldehyde-metabolizing systems in the rat gastrointestinal tract. *Alcohol and alcoholism (Oxford, Oxfordshire)*, *37*, 229-235. DOI:10.1093/alcalc/37.3.229

[24] Jones AW. (2019). Alcohol, its absorption, distribution, metabolism, and excretion in the body and pharmacokinetic calculations. *WIREs Forensic*

Science, *1*, e1340. DOI:https://doi.org/10.1002/wfs2.1340

[25] Osna NA, Donohue TM, Jr., Kharbanda KK. (2017). Alcoholic Liver Disease: Pathogenesis and Current Management. *Alcohol research : current reviews*, *38*, 147-161.

[26] Hosseini N, Shor J, Szabo G. (2019). Alcoholic Hepatitis: A Review. *Alcohol and alcoholism (Oxford, Oxfordshire)*, *54*, 408-416. DOI:10.1093/alcalc/agz036

[27] Eghtesad S, Poustchi H, Malekzadeh R. (2013). Malnutrition in liver cirrhosis:the influence of protein and sodium. *Middle East journal of digestive diseases*, *5*, 65-75.

[28] Niu X, Zhu L, Xu Y, *et al.* (2023). Global prevalence, incidence, and outcomes of alcohol related liver diseases: a systematic review and meta-analysis. *23*, 859. DOI:10.1186/s12889-023-15749-x

[29] Chiva-Blanch G, Badimon L. (2019). Benefits and Risks of Moderate Alcohol Consumption on Cardiovascular Disease: Current Findings and Controversies. *Nutrients*, *12*. DOI:10.3390/nu12010108

[30] Emberson JR, Bennett DA. (2006). Effect of alcohol on risk of coronary heart disease and stroke: causality, bias, or a bit of both? *Vascular health and risk management*, *2*, 239-249. DOI:10.2147/vhrm.2006.2.3.239

[31] Minzer S, Losno RA, Casas R. (2020). The Effect of Alcohol on Cardiovascular Risk Factors: Is There New Information? *Nutrients*, *12*. DOI:10.3390/nu12040912

[32] Tasnim S, Tang C, Musini VM, *et al.* (2020). Effect of alcohol on blood pressure. *The Cochrane database of systematic reviews*, *7*, Cd012787. DOI:10.1002/14651858.CD012787.pub2

[33] Piano MR, Phillips SA. (2014). Alcoholic cardiomyopathy: pathophysiologic insights. *Cardiovascular toxicology*, *14*, 291-308. DOI:10.1007/s12012-014-9252-4

[34] Kupari M, Koskinen P. (1998). Alcohol, cardiac arrhythmias and sudden death. *Novartis Foundation symposium*, *216*, 68-79; discussion 79-85. DOI:10.1002/9780470515549.ch6

[35] Pompili M, Serafini G, Innamorati M, *et al.* (2010). Suicidal behavior and alcohol abuse. *International journal of environmental research and public health*, *7*, 1392-1431. DOI:10.3390/ijerph7041392

[36] White AM. (2003). What happened? Alcohol, memory blackouts, and the brain. *Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism*, *27*, 186-196.

[37] Colrain IM, Nicholas CL, Baker FC. (2014). Alcohol and the sleeping brain. *Handbook of clinical neurology*, *125*, 415-431. DOI:10.1016/b978-0-444-62619-6.00024-0

[38] Curtis. CAAASA (2022). Gastroesophageal Reflux Disease. *StatPearls Publishing*.

[39] Chowdhury P, Gupta P. (2006). Pathophysiology of alcoholic pancreatitis: an overview. *World journal of gastroenterology*, *12*, 7421-7427. DOI:10.3748/wjg.v12.i46.7421

[40] Butts M, Sundaram VL, Murughiyan U, *et al.* (2023). The Influence of Alcohol Consumption on Intestinal Nutrient Absorption: A Comprehensive Review. *15*. DOI:10.3390/nu15071571

[41] Van Heertum K, Rossi B. (2017). Alcohol and fertility: how much is too much? *Fertility research and practice*, *3*, 10. DOI:10.1186/s40738-017-0037-x

[42] Testino G. (2011). The burden of cancer attributable to alcohol consumption. *Maedica*, *6*, 313-320.

[43] McDonald JA, Goyal A, Terry MB. (2013). Alcohol Intake and Breast Cancer Risk: Weighing the Overall Evidence. *Current breast cancer reports*, *5*. DOI:10.1007/s12609-013-0114-z

[44] Testino G, Leone S, Borro P. (2014). Alcohol and hepatocellular carcinoma: a review and a point of view. *World journal of gastroenterology*, *20*, 15943-15954. DOI:10.3748/wjg.v20.i43.15943

[45] Hu JX, Zhao CF, Chen WB, *et al.* (2021). Pancreatic cancer: A review of epidemiology, trend, and risk factors. *World journal of gastroenterology*, *27*, 4298-4321. DOI:10.3748/wjg.v27.i27.4298.