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Ethanol

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Abstract

Ethanol with the molecular formula C_2H_6O is a clear, colorless, volatile liquid with a pleasant smell made by fermentation of sugar. Ethanol is one of many kinds of alcohol and is the only type of alcohol that can be consumed. Apart from consumption, ethanol is used for several other purposes such as fuel to power engines, as a disinfectant (because of its bactericidal activity), as a solvent and preservative as well as serving as the primary ingredient in the preparation of alcoholic beverages. In this chapter, the author describes how ethanol is metabolized in the body, genetics behind ethanol metabolism, metabolic pathways and hosts for ethanol production, ethanol and malnutrition, why ethanol is considered as a drug and effect of ethanol on neurotransmitter [gamma-amino-butyric acid (GABA), glutamate, dopamine, and serotonin] systems. The author further explains the effect of ethanol on antidiuretic hormone (vasopressin).

Keywords: ethanol, neurotransmitters, antidiuretic hormone, GABA, glutamate, dopamine, serotonin, metabolism

1. Introduction

Ethanol is a mood-altering drug with both pleasant and unpleasant effects. It is a clear liquid that is made by the fermentation of different biological materials. Ethanol (CH_3CH_2OH) is an alcohol, a group of chemical compounds whose molecules contain a hydroxyl group, –OH, bonded to a carbon atom [1]. When an alcoholic beverage is consumed, it passes through the stomach into the small intestine where it is rapidly absorbed and distributed throughout the body. Alcohol cannot be stored in the body and therefore, the body must metabolize it to get rid of it. It can only be metabolized in the liver, where enzymes are found to initiate the process. Ethanol is metabolized in the body to provide energy and does not have any minerals, vitamins, carbohydrates, fats or protein associated with it and as a result of this, it directly contributes to malnutrition. General malnutrition is often reflected in body weight loss, mainly of adipose and muscle tissue. This loss of nutritional reserves is partly due to inadequate protein intake in the face of continued alcohol ingestion. Alcohol is very rich in energy, packing seven calories per gram. The more calories an individual consumes in alcohol, the less likely it is that the individual will eat enough food to obtain adequate nutrients. More ethanol is found in the blood and the brain than in muscle or fat tissue. Alcohol acts as a central nervous system (CNS) depressant and as a diuretic and affects several neurotransmitter systems within the brain such as glutamate, gamma-amino-butyric acid (GABA), dopamine and serotonin systems. Ethanol is also used as a fuel for internal combustion engines either alone or in combination with other fuels and has both short and long-term economic advantages over fossil fuel. One striking advantage of ethanol over other

fuel sources is that it does not cause pollution to the environment thereby reducing global warming which is caused by relentless emission of dangerous greenhouse gases emanation from use of fossil fuels.

2. Metabolism of alcohol

When an alcoholic beverage is consumed, it passes through the stomach into the small intestine where the ethanol is rapidly absorbed and distributed throughout the body and more ethanol is found in the blood and the brain than in muscle or fat tissue. Around 2–8% of consumed alcohol is lost through urine, sweat, or the breath and the other 92–98% is metabolized in the liver. Alcohol is metabolized by several pathways. These pathways involves four enzymes—alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH), catalase and microsomal ethanol oxidizing system (MEOS). These enzymes help break apart the alcohol molecule, making it possible to eliminate it from the body. In the first step, the primary pathway for alcohol metabolism involves alcohol dehydrogenase (ADH), a cytosolic enzyme that catalyzes the conversion of alcohol to acetaldehyde, a highly toxic substance and known carcinogen [2] (**Figure 1**). ADH is found mainly in the liver but can also be found in other organs of the body such as brain and stomach. During the process of conversion of ethanol to acetaldehyde, ethanol binds to alcohol dehydrogenase enzyme and loses some of its electrons in the form of hydrogen atoms to a coenzyme nicotinamide adenine dinucleotide (NAD) to form NADH. Ethanol oxidation generates an excess of reducing equivalents in the liver, mainly as NADH. NADH participates in numerous metabolic reactions in the body and for proper functioning of the body; the ratio of NAD to NADH must be tightly controlled. The conversion of ethanol to acetaldehyde by alcohol dehydrogenase enzyme reduces the cellular NAD to NADH ratio and this has profound effects on other liver metabolic pathways that require NAD or are inhibited by NADH. Decreased NAD/NADH ratio inhibits important reactions in the body such as glycolysis, tricarboxylic acid cycle (TCA cycle), fatty acid oxidation, pyruvate
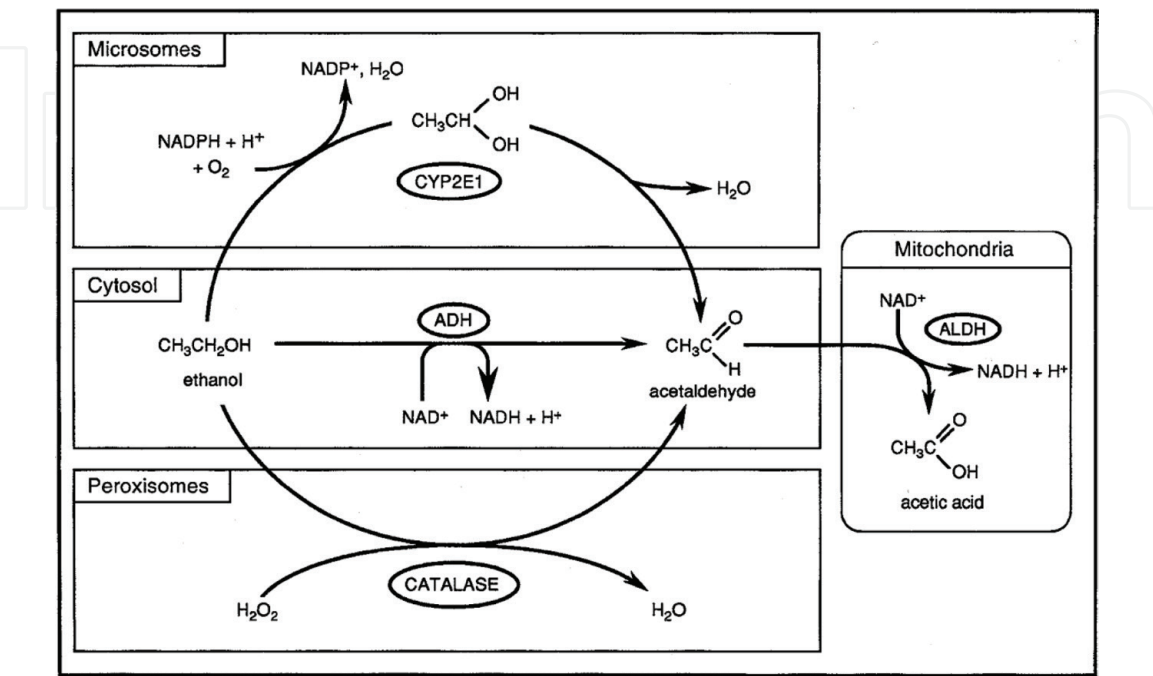

Figure 1.
Metabolism of ethanol to acetic acid/acetate.

dehydrogenase and gluconeogenesis. Altered NAD/NADH ratio/elevated cellular NADH levels may lead to several metabolic disorders. Elevated levels of NADH could lead to the formation of abnormally high levels of lactic acid, which in turn reduces the capacity of the kidney to excrete uric acid. Excessive uric acid in the body can lead to gout, a disorder characterized by extremely painful swelling of joints [3]. Increased NADH promotes the generation of the building blocks of fat molecules (fatty acids) and reduces the breakdown of fats in the liver, thereby contributing to fat accumulation in that organ [4]. The resulting fatty liver is the earliest stage and the most common form of alcohol-induced liver disease. The elevation in NADH levels resulting from the ADH-mediated breakdown of alcohol also may play a role in the formation of scar tissue that characterizes fibrosis, a more severe stage of liver disease.

Another pathway is the microsomal ethanol oxidizing system (MEOS). The primary component of the MEOS is the cytochrome P450, which exists in several variants. The variant most important for alcohol metabolism is cytochrome P450 2E1 (CYP2E1) [5]. This pathway uses NADPH as a coenzyme in the metabolism of ethanol and results in the formation of NADP and water (**Figure 1**). The cytochrome CYP2E1/MEOS pathway is only active after a person has consumed large amounts of alcohol [6]. Alcohol breakdown by microsomal ethanol oxidizing system generates several highly reactive oxygen-containing molecules called reactive oxygen species (ROS). These reactive oxygen species can damage liver cells by inactivating essential enzymes and altering the breakdown of fat molecules and when there is an imbalance between ROS and antioxidant systems, a condition known as oxidative stress sets in which can cause liver cell damage. Alcohol and its metabolism have been shown to reduce the levels of both glutathione (GSH) and vitamin E (α-tocopherol) which protects the body against ROS [6]. The catalase pathway metabolizes only a small fraction of alcohol in the body [2].

In the second step, acetaldehyde is further metabolized down by aldehyde dehydrogenase (ALDH) to another less active by product called acetate (**Figures 2** and **3**) which in turn is broken down into carbon dioxide and water. Ethanol is mainly eliminated from the body via metabolism into carbon dioxide and water. Acetate/acetic acid combine with Coenzyme A to form acetyl-CoA. The acetyl-CoA enters the tricarboxylic acid (TCA) cycle/Krebs cycle. In the Krebs cycle, acetate in the form of acetyl CoA is broken down into carbon dioxide and in this process ATP is formed (**Figure 3**) [2]. Some individuals have less effective forms of ethanol metabolizing enzymes and can experience more marked symptoms from ethanol consumption than others [7].
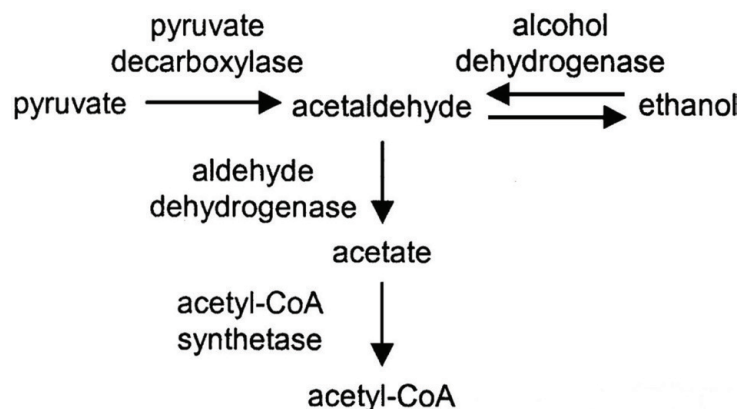

Figure 2.
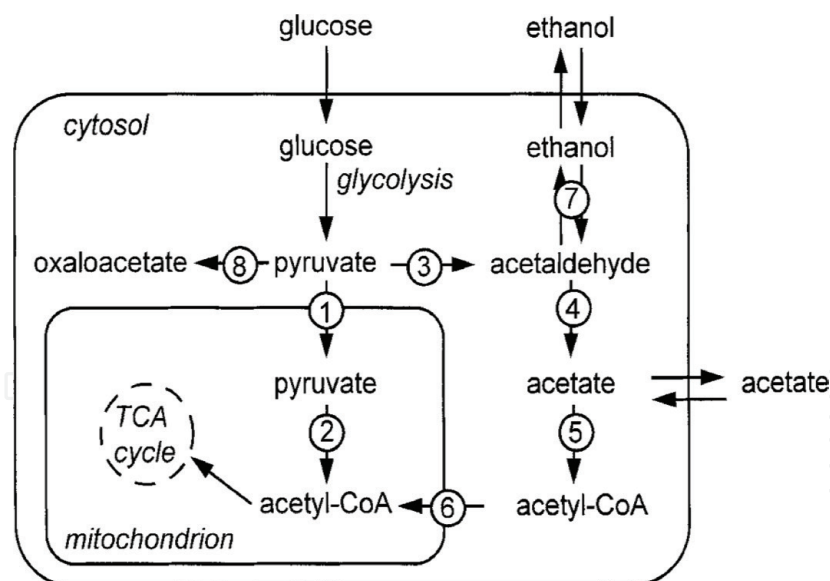*Acetaldehyde dehydrogenases in ethanol and pyruvate metabolism.*

Figure 3.
Metabolism of ethanol to acetyl CoA. Numbered reactions are catalyzed by the following enzymes: 1: mitochondrial pyruvate carrier; 2: pyruvate dehydrogenase complex; 3: pyruvate decarboxylase; 4: acetaldehyde dehydrogenase; 5: acetyl-CoA synthetase; 6: carnitine shuttle; 7: alcohol dehydrogenase; 8: pyruvate carboxylase.

3. Genetics behind ethanol metabolism

Important factors that can influence responses to alcohol are variations in alcohol-metabolizing enzymes. Genetically influenced metabolic factors have been implicated in the etiology of alcoholism among different ethnic groups. Several genetically determined variants of ADH and ALDH enzymes exist that differ in their level of activity and different people have different variants of these enzymes. Some of these enzyme variants work more or less efficiently than others; this means that some people can break down ethanol to acetaldehyde, or acetaldehyde to acetate, more quickly than others. The type of ADH and ALDH an individual carries has been shown to influence how much he or she drinks, which in turn influences his or her risk for developing alcoholism [8].

Genetic differences in ADH and ALDH enzymes may help to explain why some ethnic groups have higher or lower rates of alcohol-related problems. There are multiple ADH and ALDH enzymes that are encoded by different genes. These genes occur in several variants and the enzymes encoded by these alleles can differ in the rate at which they metabolize ethanol or acetaldehyde or in the levels at which they are produced and these variants have been shown to influence a person's drinking levels and consequently the risk of developing alcohol abuse or dependence [8]. Studies have shown that people carrying certain ADH and ALDH alleles are at significantly reduced risk of becoming alcohol dependent. The mechanism through which ADH and ALDH variants influence alcoholism risk is thorough the elevation of acetaldehyde levels, resulting either from a more rapid ethanol oxidation or from slower acetaldehyde oxidation. Acetaldehyde is a toxic substance whose accumulation leads to a highly aversive reaction.

Humans have seven different ADH genes called ADH1A, ADH1B, ADH1C, ADH4, ADH5, ADH6, and ADH7 and there are three different ADH1B alleles: the ADH1B*1 allele, ADH1B*2 (this allele is common in Asians) and the ADH1B*3 (this allele primarily is found in people of African descent) alleles. The ADH1B*2 allele is associated with rapid ethanol oxidation and has shown protective effects against alcohol dependence in a variety of populations and ethnic groups. ADH1B*2 allele is found at high frequency in East Asians and it has been shown to be protective against alcoholism [8, 9]. ADH1B*2 allele is not very common in European or

African populations but also provides protection against alcoholism [10]. ADH1B*2 allele is found at moderate frequencies among people of Jewish descent and reduces binge drinking and risk for alcoholism [11, 12]. The protective effect of ADH1B*2 appears to be weaker in European than in Asian populations [10]. This difference could result from different social and environmental factors. The ADH1B*3 allele had a significant protective effect on risk for alcoholism in a set of African-American families selected for having multiple alcoholic members [13].

Numerous polymorphisms exist in the human ALDH genes, some of which cause inborn errors of metabolism and contribute to clinically relevant diseases [14]. Several isozymes of ALDH have been identified, but only the cytosolic ALDH1 and the mitochondrial ALDH2 metabolize acetaldehyde produced during ethanol oxidation [8, 15]. Polymorphism in the ALDH2 gene is associated with altered acetaldehyde metabolism, alcohol-induced 'flushing' syndrome, decreased risk for alcoholism and increased risk of ethanol-induced cancers. Genetic polymorphism of the ALDH2 gene result in allelic variants ALDH2*1 and ALDH2*2. ALDH2*2 allele is relatively common in people of Chinese, Japanese, and Korean descent but is essentially absent in people of European or African descent [8, 16]. People carrying an ALDH2*2 allele show an alcohol flush reaction, even when they consume only relatively small amounts of alcohol [17]. In these people, acetaldehyde levels in the blood increase from nearly undetectable levels to levels high enough to trigger the highly aversive reactions.

4. Metabolic pathways and hosts for ethanol production

Ethanol is produced from glucose via fermentative consumption of pyruvate, the end product of glycolysis [18]. Glycolysis is a metabolic process that converts glucose to pyruvate while producing ATP. The pyruvate formed by glycolysis is further metabolized via one of the three catabolic routes. In aerobic organisms or tissues, under aerobic conditions, pyruvate is oxidized with the loss of its carboxyl group as CO_2 to yield the acetyl-CoA; the acetyl-CoA is then completely oxidized to CO_2 in the citric acid cycle (**Figure 4**). The second route for pyruvate is its reduction to lactate via lactic acid fermentation in vigorously contracting muscle. Under anaerobic condition, pyruvate is reduced to lactate. Another major route of pyruvate catabolism leads to ethanol. In some plant tissues and certain invertebrates, protists and microorganisms such as brewer's yeast, pyruvate under anaerobic conditions can be fermented to ethanol by sequential reactions of pyruvate decarboxylase (PDC) and alcohol dehydrogenase (ADH) (**Figure 4**).

Microbial fermentation was introduced by Louis Pasteur in the late 1850s and was the first to recognize the relationship between the presence of yeast cells and the conversion of sugar to ethanol. Today ethanol producing *Saccharomyces cerevisiae* (yeast) have been exploited to produce a wide variety of alcoholic beverages and biofuels. Many microorganisms are being used for ethanol and biofuel production, but all have certain limitations such as industrial robustness, substrate utilization, productivity and yield. *Saccharomyces cerevisiae* (yeast) is a leading traditional industrial biocatalyst microorganism for ethanol production and with technological advancement in genetic engineering, bacteria such as *Escherichia coli*, *Zymomonas mobilis*, *Corynebacterium glutamicum* and *Bacillus subtilis* have been developed [19].

Zymomonas mobilis (*Z. mobilis*), a bacterium commonly found in plant saps and in honey has many desirable industrial biocatalyst characteristics and has been suggested as an alternative to the classical model, *Saccharomyces cerevisiae* (yeast) due to its advantage for ethanol yield. *Saccharomyces cerevisiae* uses the Embden-Meyerhof-Parnas (EMP) pathway for glycolysis while *Z. mobilis* uses the Entner-Doudoroff
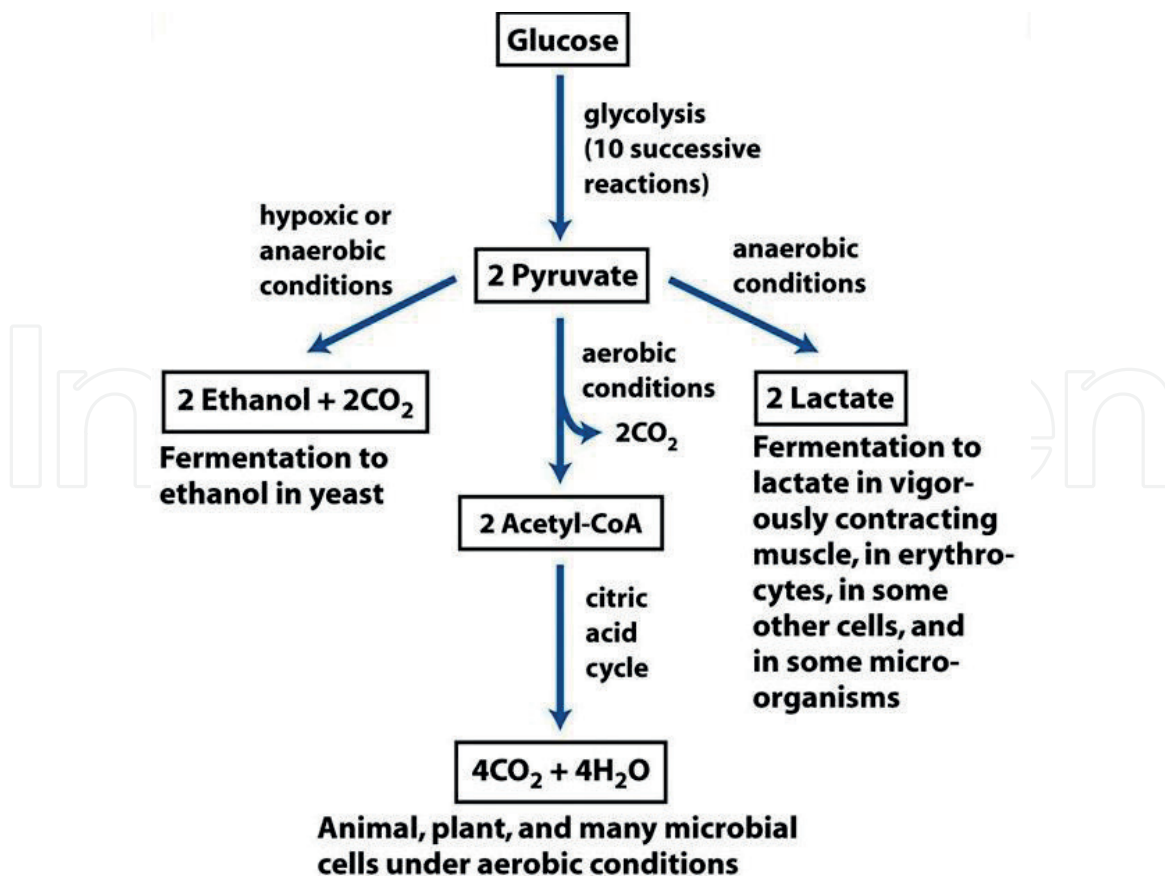
Figure 4.
Three possible catabolic fates of pyruvate formed in glycolysis (adapted from Lehninger principles of biochemistry).

(ED) pathway. The ED pathway is found in strict aerobic microorganisms and conducts fermentation with 50% less ATP produced relative to the EMP pathway, which leads to improved ethanol yield. Moreover, *Z. mobilis* has a high-specific cell surface area and consumes glucose faster than *S. cerevisiae*, leading to higher ethanol productivity than *S. cerevisiae* [20] (**Figure 5**). Although the EMP pathway is a major glycolytic route in most eukaryotes and prokaryotes, glycolytic pathways are much more diverse in prokaryotes [21]. Among different glycolytic pathways, the ED and EMP pathways are the most abundant pathway for glycolysis [21]. Two molecules of ATP are produced from each molecule of glucose consumed using EMP pathway, while the ED pathway produces only one ATP molecule from one glucose molecule. Given that ATP is tightly coupled with anabolism and cell growth, ED pathway-utilizing *Z. mobilis* produces less energy than EMP pathway-dependent species such as *S. cerevisiae* and consequently, *Z. mobilis* has more available carbons for ethanol fermentation with 2.5-fold higher specific ethanol productivity than that of *S. cerevisiae* [22].

Z. mobilis is an obligately fermentative bacterium which lacks a functional system for oxidative phosphorylation. Like the *Saccharomyces cerevisiae*, *Z. mobilis* produces ethanol and carbon dioxide as principal fermentation products. Ethanol is produced by *Z. mobilis* using a short pathway which requires two enzymatic activities: pyruvate decarboxylase and alcohol dehydrogenase. Pyruvate decarboxylase is the key enzyme in this pathway which diverts the flow of pyruvate to ethanol. In this pathway, the non-oxidative decarboxylation of pyruvate to produce acetaldehyde and carbon dioxide is catalyzed by pyruvate decarboxylase. In *Z. mobilis*, two alcohol dehydrogenase isozymes are present which catalyzes the reduction of acetaldehyde to ethanol during fermentation.
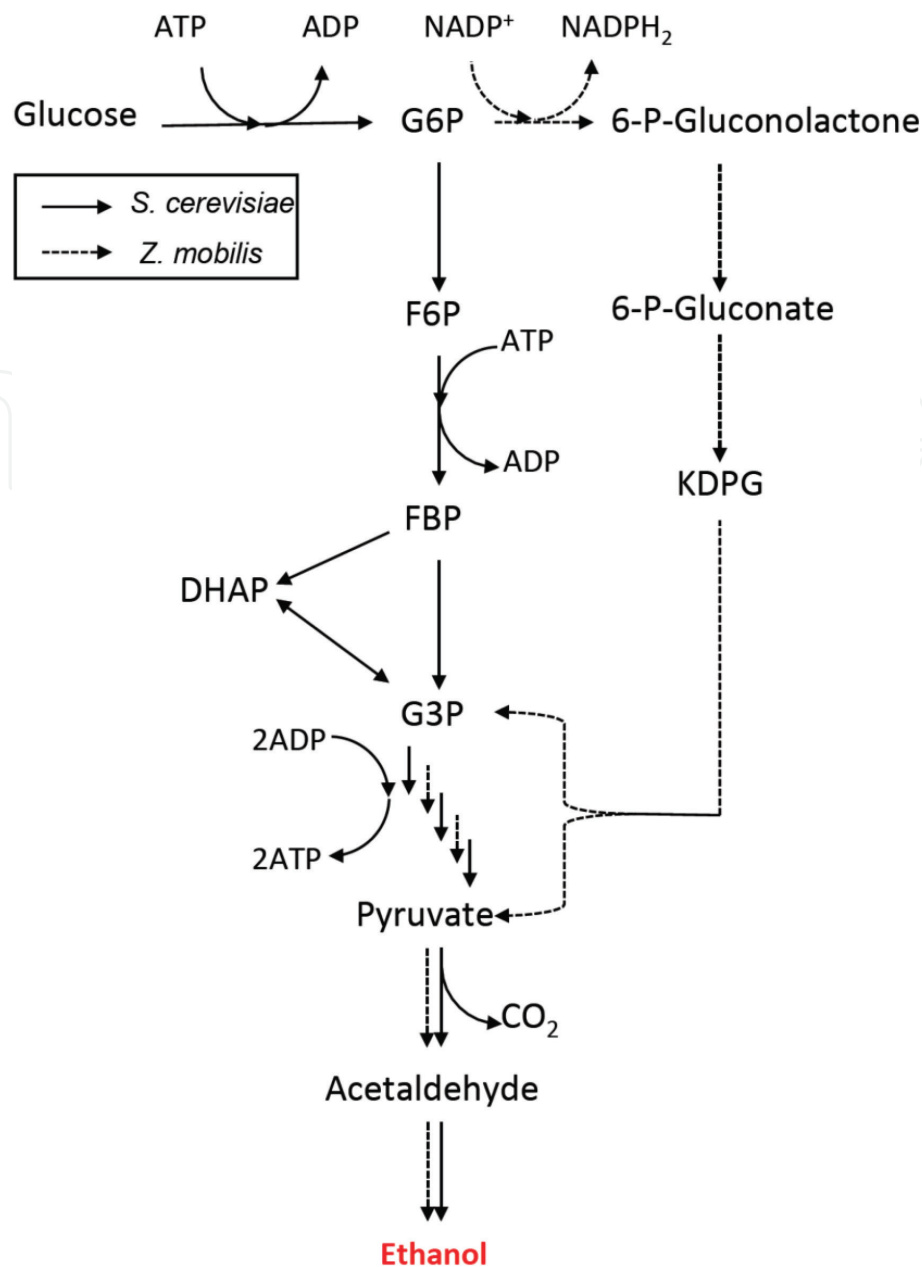
Figure 5.
Ethanol fermentation pathways in S. cerevisiae and Z. mobilis (solid line: EMP glycolysis pathway; dashed line: ED glycolysis pathway). KDPG: 2-keto-3-deoxy-6-phosphogluconate; G6P: glucose 6-phosphate; F6P: fructose 6-phosphate; FBP: fructose 1,6-bisphosphate; DHAP: dihydroxyacetone phosphate; G3P: glyceraldehyde 3-phosphate.

5. Ethanol and malnutrition

Ethanol consumption has an effect on person's nutritional status. Many people who consume one to two glasses or less of alcoholic beverages per day consider those beverages a part of their normal diet and acquire a certain number of calories from them. When consumed in excess, ethanol can interfere with the nutritional status of the consumer. Ethanol can alter the intake, absorption and utilization of various nutrients [23, 24]. The primary constituents of alcoholic beverages are water, ethanol (alcohol), sugars (carbohydrates) and negligible amounts of other nutrients like proteins, vitamins and minerals. Because alcoholic beverages provide almost no nutrients, they are considered as "empty calories". Any calories provided by alcoholic beverages are derived from the carbohydrates and alcohol they contain. Ethanol has a caloric value of 7.1 kcal/g.

Many consumers of alcoholic beverages suffer from various degrees of malnutrition (both primary and secondary malnutrition). A situation where alcohol replaces other nutrients in the diet resulting in overall reduced nutrient intake is known as primary malnutrition while secondary malnutrition occurs when alcoholics consumes adequate nutrients but alcohol interferes with the absorption of those nutrients from the intestine so they are not available to the body [25]. The risk of developing micro- and macronutrient deficiencies increases significantly when alcohol makes up more than 30% of total caloric intake [26]. Heavy alcohol consumption not only influences the drinker's diet but also affects the metabolism of those nutrients that are consumed. Even if the drinker ingests sufficient proteins, fats, vitamins, and minerals, deficiencies may develop if those nutrients are not adequately absorbed from the gastrointestinal tract into the blood, are not broken down properly, and/or are not used effectively by the body's cells.

Proteins are essential nutrients for the human body that help maintain the cell's structure, act as enzymes that mediate almost all biochemical processes/reactions occurring in the body and transport certain substances in the body. Amino acids are building blocks of proteins and proteins are composed of 20 different amino acids. Some of these amino acids can be made by the body itself (non-essential amino acids) from various precursors or are recycled when proteins that are damaged or are no longer needed are broken down or degraded. Other amino acids cannot be produced by the body and must be obtained through diet (essential amino acids). Heavy alcohol consumption can interfere with the production and uptake of these non-essential and essential amino acids. Vitamins are micronutrients present in food essential for normal metabolism and insufficient levels of vitamin in the body can lead to serious health consequences. Alcoholics tends to have deficiencies in certain vitamins particularly thiamine (vitamin B1), riboflavin (vitamin B2), pyridoxine (vitamin B6), ascorbic acid (vitamin C) and folic acid.

6. Ethanol as a psychoactive drug and its effect on neurotransmitters

Ethanol is a psychoactive substance which is present as the active ingredient in alcoholic beverages such as beer, wine, and distilled spirits [27]. Ethanol consumption produces mood lift and euphoria, decreased anxiety, increased sociability, sedation, impairment of cognitive, memory, motor, and sensory function, and slows down the activity (depressant) of the central nervous system (CNS) and because of its psychoactive effects, it is considered a drug. Psychoactive substances are those substances that act on the nervous system to alter states of consciousness, modify perceptions and change moods. Psychoactive drugs are classified into depressants, stimulants and hallucinogens. Depressants slow down physical and mental activity; Stimulants increases the activity of the central nervous system while Hallucinogens modify perceptions and produce unusual visual images.

Human behaviors and emotions are modulated by neurotransmitters that act as keys between neurons. Ethanol has been shown to affect a variety of neurotransmitters in the CNS. A neurotransmitter is a chemical that helps transmit messages from cell to cell within the nervous system and are crucial to muscle control, influences thought processes, memory and emotion. Alcohol mainly affects the nerve cells in the brain, causing interference between communication of these cells and other cells throughout the body. This interference restrains the activities of the excitatory nerve pathways and increases the activities of inhibitory nerve pathways. Alcohol affects several neurotransmitter systems—those for GABA, glutamate, serotonin and dopamine. Alcohol is an agonist for GABA, serotonin and dopamine—it increases their activity and is an antagonist for glutamate—it reduces glutamate activity.

Neurotransmitters interact with receptors on the dendrites of the other neuron and have specific shapes that fit into a receptor that can accommodate that shape. Once the neurotransmitter and the receptor are connected, the neurotransmitter sends information to the next neuron to either fire an action potential, or to inhibit firing (**Figure 6**). Neurotransmitters can either be excitatory or inhibitory according to the effect they have on the second neuron once they are released into the synaptic gap. Excitatory neurotransmitter triggers depolarization, increasing the likelihood of a response while inhibitory neurotransmitter triggers hyperpolarization, decreasing the likelihood of a response. Excitatory and inhibitory synaptic transmission use different neurotransmitters and receptors. Excitatory synaptic transmission uses a neurotransmitter called glutamate. Glutamate is a common amino acid used in the body to build proteins. In the central nervous system, it is the major excitatory neurotransmitter where it interacts with glutamate receptors in the post-synaptic neuron. These receptors are ion channels that are permeable to sodium ions (Na^+) and thus generate an action potential. Excitatory synaptic transmission also uses other neurotransmitter like acetylcholine, nitric oxide and catecholamines (norepinephrine, epinephrine and dopamine).

Inhibitory synaptic transmission uses a neurotransmitter called gamma-amino butyric acid (GABA). This interacts with GABA receptors, ion channels that are permeable to negatively charged chloride ions and opening of these channels makes it harder for a neuron to generate an action potential. Inhibitory synaptic transmission also uses serotonin, glycine and taurine as neurotransmitter. The main inhibitory neurotransmitter in the brain is GABA [28] and two major subtypes of GABA receptor have been described. The $GABA_A$ receptor family of ligand-gated ion channels consists of pentameric complexes containing binding sites for GABA agonists and other agent. The $GABA_A$ receptor complex regulates chloride ion flux through a coupled chloride channel and ethanol is widely reported to increase the activation of $GABA_A$ receptors.

Ethanol is an indirect GABA agonist and psychotropic depressant of the CNS [29]. This property is associated with the action of alcohol on different neurotransmitters, including the stimulation of gamma-amino butyric acid and the inhibition of glutamate, the main central excitatory neurotransmitter. Alcohol potentiates the effects of GABA by acting directly on its receptors, enhancing their inhibitory effect which includes sedation, loss of inhibitions and relaxation [30]. The mechanism
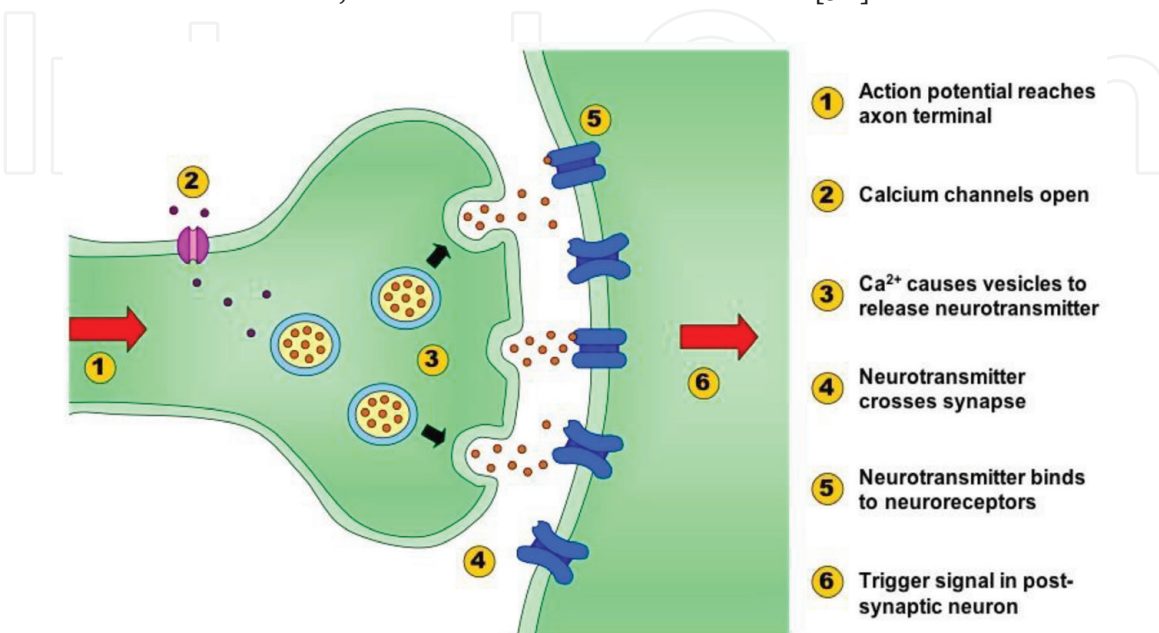

1 Action potential reaches axon terminal
2 Calcium channels open
3 Ca^{2+} causes vesicles to release neurotransmitter
4 Neurotransmitter crosses synapse
5 Neurotransmitter binds to neuroreceptors
6 Trigger signal in post-synaptic neuron

Figure 6.
Neuron-neuron interaction—transmission of impulse across the synapse.

by which ethanol enhances $GABA_A$ inhibitory currents involved a hyperpolarizing shift in the $GABA_A$ inhibitory postsynaptic current (IPSC) reversal potential in cortex neurons and increasing the amplitude of $GABA_A$ receptor-mediated conductance in septal neurons [31]. When $GABA_A$ receptor activation is enhanced by ethanol, it may involve enhancement of the initial peak of Cl^- current through the channel rather than the sustained component of channel opening [32]. The enhancement of the $GABA_A$ receptor activation by ethanol may be modulated, in part, by protein kinase C (PKC) [33].

Glutamate is a major excitatory neurotransmitter in the brain that exerts its effects through several receptor subtypes, including the N-methyl-D-aspartate (NMDA) receptor. Unlike the case with GABA, alcohol inhibits glutamate activity in the brain. In a region of the brain called striatum which contains the nucleus accumbens, ethanol exposure causes a drop in the extra cellular glutamate levels [34]. Following acute administration ethanol, glutamate mediated signal transmission is suppressed in the central nucleus of the amygdala and this effect is enhanced following chronic alcohol exposure [35]. Ethanol inhibits ionotropic glutamate, amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and kainate receptors activity in the brain and N-methyl-D-aspartate (NMDA) receptors are the major target of ethanol's inhibitory action. Ethanol also inhibits the induction of neural plasticity in many brain regions including the dorsal and ventral striatum as a result of inhibitory effects on ionotropic receptors, especially the NMDA receptors [36, 37].

Serotonin is a monoamine neurotransmitter known as 5-HT, a derivative of tryptophan and is extensively found in the gastrointestinal tract, platelets and the CNS. Serotonin plays a role in many brain processes, including regulation of body temperature, sleep, mood, appetite, pain and modulates behavioral response to unfairness [38]. Defect with the serotonin pathway can cause obsessive-compulsive disorder, anxiety disorders and depression. Most of the drugs used to treat depression today work by increasing serotonin levels in the brain [39]. Alcohol increases serotonin release in the nervous system. Increase in concentrations of serotonin in the urine and blood have been observed after taking alcohol. Alcohol exposure alters various aspects of serotonin's synaptic functions and also interferes with the function of serotonin receptors including the $5\text{-}HT_{1A}$, $5\text{-}HT_{1B}$, $5\text{-}HT_2$, and $5\text{-}HT_3$ receptors. Each subtype of serotonin receptors has its own specific influence on behavior related to the consumption of alcohol [40]. $5\text{-}HT_{1A}$ may control consummatory behavior, including alcohol consumption while $5\text{-}HT_{1B}$ may contribute not only to alcohol's intoxicating effects, but also influence the development of tolerance to alcohol. $5\text{-}HT_2$ plays a role in alcohol's rewarding effects and contributes to the development of alcohol withdrawal symptoms while $5\text{-}HT_3$ has a part in regulating alcohol consumption. Serotonin also affects other neurotransmitters. For example, alcohol-facilitated serotonin may affect the GABA system [41]. Similarly, alcohol-influenced serotonin works to stimulate increased dopamine production and, thus, increased emotional behavior [42].

Dopamine is a neurotransmitter primarily involved in a circuit called the mesolimbic system, which projects from the brain's ventral tegmental area to the nucleus accumbens. It is an excitatory neurotransmitter in the catecholamine family responsible for modulating reward and pleasure. It plays a key role in regulating emotional responses, the reward seeking processes and movement. Several lines of evidence converge to demonstrate that the dopaminergic mesolimbic system plays a significant part in the motivational and reinforcement mechanisms related to behaviors that are vital to survival [43]. Alcohol increases dopaminergic transmission in the mesolimbic pathway and increases the firing rate of dopaminergic neurons, which enhances the amount of dopamine released in the core of the system.

7. Effect of ethanol on antidiuretic hormone (vasopressin)

Vasopressin is an antidiuretic hormone that plays a major role in the regulation of water excretion. The posterior pituitary gland releases vasopressin in response to a fall in blood volume or a rise in plasma osmolality and acts to conserve water by increasing the permeability of water to the distal convoluted tubules and collecting tubules in the renal nephrons through insertion of aquaporin-2 channels into the apical membrane of the tubular epithelial cells [44]. Ingestion of alcohol does increase plasma osmolality, but alcohol also acts directly to inhibit the release of vasopressin, independent of plasma osmolality. Once ethanol is consumed, it is distributed in the blood, brain and muscle tissues. Alcohol is a diuretic that affects five centers in the brain namely the cerebral cortex, limbic system, cerebellum, hypothalamus and pituitary gland and the medulla. The hypothalamus controls the automatic functions of the brain and coordinates endocrine functions through nerve impulse actions on the pituitary gland. Ethanol affects hypothalamus and pituitary gland by increasing urine excretion; inhibiting the pituitary secretion of anti-diuretic hormone (ADH), which makes the kidney reabsorb water. When the ADH levels are decreased, the kidney does not reabsorb water from the urine which results in the kidney producing more urine.

8. Conclusion

In conclusion, ethanol is a powerful drug that affects several neurological pathways such as the dopaminergic, serotoninergic, γ-amino butyric acid (GABA) and glutamate pathways and causes significant changes in the brain. It also affects the central nervous system and acts to depress brain functions, very much in the style of an anesthetic. Ethanol at low blood concentrations releases behaviors that are otherwise inhibited and usually produces feelings of relaxation and good mood which may facilitate socializing. Thus at low doses, ethanol is possibly useful but caution however needs to be exercised as even low quantities of alcohol affect the ability of the brain (hippocampus) to process information, which in turn impairs memory formation. Higher doses of alcohol affect the brain further by inducing intoxication wherein the person may experience temporary loss of coordination and judgment. Long-term alcohol abuse produces physiological changes in the brain and these changes in the brain chemistry maintain the alcoholic's compulsive inability to cease alcohol consumption being fully aware of the harm caused by alcohol and results in alcohol withdrawal syndrome upon discontinuation of alcohol.

Conflict of interest

I have no conflict of interest to declare.

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References

[1] National Center for Biotechnology Information. PubChem Compound Database; CID=702, https://pubchem.ncbi.nlm.nih.gov/compound/702 (accessed March 03, 2018)

[2] National Institute on Alcohol Abuse and Alcoholism. Alcohol Alert: Alcohol Metabolism. No. 35, PH 371. Bethesda, MD: The Institute; 1997 Available from: http://pubs.niaaa.nih.gov/publications/aa35.htm

[3] Lieber CS. Hepatic and other medical disorders of alcoholism: From pathogenesis to treatment. Journal of Studies on Alcohol. 1998;**59**:9-25

[4] Lieber CS, Schmid R. The effect of ethanol on fatty acid metabolism: Stimulation of hepatic fatty acid synthesis in vitro. Journal of Clinical Investigation. 1961;**40**:394-399

[5] Salmela KS, Kessova IG, Tsyrlov IB, Lieber CS. Respective roles of human cytochrome P-4502E1, 1A2 and 3A4 in the hepatic microsomal ethanol oxidizing system. Alcoholism: Clinical and Experimental Research. 1998;**22**:2125-2132

[6] Lieber CS. Relationships between nutrition, alcohol use, and liver disease. Alcohol Research & Health. 2003;**27**(3):220-231

[7] Agarwal DP, Goedde HW. Pharmacogenetics of alcohol metabolism and alcoholism. Pharmacogenetics. 1992;**2**(2):48-62

[8] Hurley TD, Edenberg HJ, Li TK. The pharmacogenomics of alcoholism. In: Pharmacogenomics: The Search for Individualized Therapies. Weinheim, Germany: Wiley-VCH; 2002. pp. 417-441

[9] Chen HJ, Tian H, Edenberg HJ. Natural haplotypes in the regulatory sequences affect human alcohol dehydrogenase 1C (ADH1C) gene expression. Human Mutation. 2005;**25**(2):150-155

[10] Whitefield JB. Alcohol dehydrogenase and alcohol dependence: Variation in genotype-associated risk between populations. American Journal of Human Genetics. 2002;**71**(5):1247-1250

[11] Luczak SE, Shea SH, Carr LG, Li T, Wall TL. Binge drinking in Jewish and non-Jewish white college students. Alcoholism: Clinical and Experimental Research. 2002;**26**(12):1773-1778

[12] Hasin ND, Aharonovich E, Liu X, Mamman Z, Matseoane K, Carr L, Li T. Alcohol and ADH2 in Israel: Ashkenazis, Sephardics, and recent Russian immigrants. American Journal of Psychiatry. 2002;**159**(8):1432-1434

[13] Edenberg HJ, Foroud T. The genetics of alcoholism: Identifying specific genes through family studies. Addiction Biology. 2006;**11**(3-4):386-396

[14] Vasiliou V, Pappa A. Polymorphisms of human aldehyde dehydrogenases. Consequences for drug metabolism and disease Pharmacology. 2000;**61**(3):192-198

[15] Crabb DW, Edenberg HJ, Bosron WF, Li TK. Genotypes for aldehyde dehydrogenase deficiency and alcohol sensitivity: The inactive ALDH2(2) allele is dominant. Journal of Clinical Investigation. 1989;**83**:314-316

[16] Oota H, Pakstis AJ, Bonne-Tamir B. The evolution and population genetics of the ALDH2 locus: Random genetic drift, selection, and low levels of recombination. Annals of Human Genetics. 2004;**68**(Pt. 2):93-109

[17] Peng GS, Yin JH, Wang MF, Lee JT, Hsu YD, Yin SJ. Alcohol sensitivity in Taiwanese men with different alcohol and aldehyde dehydrogenase genotypes. Journal of the Formosan Medical Association. 2002;**101**(11):769-774

[18] Ingram LO, Conway T, Clark DP, Sewell GW, Preston JF. Genetic engineering of ethanol production in *Escherichia coli*. Applied and Environmental Microbiology. 1987;**53**:2420-2425

[19] Dien BS, Cotta MA, Jeffries TW. Bacteria engineered for fuel ethanol production: Current status. Applied Microbiology and Biotechnology. 2003;**63**:258-266

[20] Conway T. The Entner-Doudoroff pathway: History, physiology and molecular biology. FEMS Microbiology Reviews. 1992;**9**:1-27

[21] Flamholz A, Noor E, Bar-Even A, Liebermeister W, Milo R. Glycolytic strategy as a tradeoff between energy yield and protein cost. Proceedings of the National Academy of Sciences of the United States of America. 2013;**110**:10039-10044

[22] Weber C, Farwick A, Benisch F, Brat D, Dietz H, Subtil T, Boles E. Trends and challenges in the microbial production of lignocellulosic bioalcohol fuels. Applied Microbiology and Biotechnology. 2010;**87**:1303-1315

[23] Lieber CS. Alcohol: Its metabolism and interaction with nutrients. Annual Review of Nutrition. 2000;**20**:395-430

[24] Lieber CS. Hepatic, metabolic and toxic effects of ethanol: 1991 update. Alcoholism: Clinical and Experimental Research. 1991;**15**:573-592

[25] Lieber CS. Alcohol-nutrition interactions. In: Li TK, Schenker S, Lumeng L, editors. Alcohol and Nutrition:

Proceedings of a Workshop. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 1979. pp. 47-63

[26] Tanaka Y, Funaki N, Mak IM, Kim C-I, Lieber CS. Effects of ethanol and hepatic vitamin A on the proliferation of lipocytes in regenerating rat liver. Journal of Hepatology. 1991;**12**:344-350

[27] Collins SE, Kirouac M. Alcohol consumption. Encyclopedia of Behavioral Medicine. 2013;**2013**:61-65

[28] Curtis DR. GABA synapses in the brain. Trends in Neurosciences. 1995;**18**:263

[29] Haes TM, Clé DV, Nunes TF, Roriz-Filho JS, Moriguti JC. Alcohol and central nervous system. Medicina (Ribeirão Preto). 2010;**43**(2):153-163

[30] Charlton ME, Sweetnan PM, Fitzgerald LW, Terwilliger RZ, Nestler EJ, Duman RS. Chronic ethanol administration regulates the expression of GABAA, receptor α 1 and α 5 subunit in the ventral tegmental area and hippocampus. Journal of Neurochemistry. 2002;**68**(1):121-127

[31] Soldo BL, Proctor WR, Dunwiddie TV. Ethanol differentially modulates GABAA receptor-mediated chloride currents in hippocampal, cortical, and septal neurons in rat brain slices. Synapse. 1994;**18**:94-103

[32] Nishio M, Narahashi T. Ethanol enhancement of GABA-activated chloride current in rat dorsal root ganglion neurons. Brain Research. 1990;**518**:283-286

[33] Weiner JL, Zhang L, Carlen PL. Potentiation of GABAA mediated synaptic current by ethanol in hippocampal CA1 neurons: Possible role of protein kinase CJ. Journal of Pharmacology and Experimental Therapeutics. 1994;**268**:1388-1395

[34] Carboni S, Isola R, Gessa GL, Rossetti ZL. Ethanol prevents the glutamate release induced by N-methyl-D-aspartate in the rat striatum. Neuroscience Letters. Mar 2, 1993;**152**(1-2):133-136

[35] Roberto M, Schweitzer P, Madamba SG, Stouffer DG, Parsons LH, Siggins GR. Acute and chronic ethanol alter glutamatergic transmission in rat central amygdala: An in vitro and in vivo analysis. The Journal of Neuroscience. Feb 18, 2004;**24**(7):1594-1603

[36] Lovinger DM, White G, Weight FF. Ethanol inhibits NMDA-activated ion current in hippocampal neurons. Science. Mar 31, 1989;**243**(4899):1721-1724

[37] Nie Z, Madamba SG, Siggins GR. Ethanol inhibits glutamatergic neurotransmission in nucleus accumbens neurons by multiple mechanisms. The Journal of Pharmacology and Experimental Therapeutics. 1994;**271**:1566-1573

[38] Crockett MJ, Clark L, Tabibnia G, Lieberman MD, Robbins TW. Serotonin modulates behavioral reactions to unfairness. Science. Jun 27, 2008;**320**(5884):1739

[39] Benmansour S, Cecchi M, Morilak DA, Gerhardt GA, Javors MA, Gould GG, Frazer A. Effects of chronic antidepressant treatments on serotonin transporter function, density, and mRNA level. The Journal of Neuroscience. 1999;**19**(23): 10494-10501

[40] Lovinger DM. The role of serotonin in alcohol's effects on the brain. Current Separations. 1999;**18**:23-28

[41] Samson HH, Harris RA. Neurobiology of alcohol abuse. Trends in Pharmacological Science. 1992;**13**:206-211

[42] Campbell AD, Kohl RR, McBride WJ. Serotonin-3 receptor and ethanolstimulated somatodendritic dopamine release. Alcohol. 1996;**13**:569-574

[43] Dulawa SC, Grandy DK, Low MJ, Paulus MP, Geyer MA. Dopamine D4 receptor-knock-out mice exhibit reduced exploration of novel stimuli. The Journal of Neuroscience. 1999;**19**:9550-9556

[44] Boone M, Deen PMT. Physiology and pathophysiology of the vasopressin-regulated renal water reabsorption. Pflügers Archiv. 2008;**456**:1005-1024