A REVIEW ON ALCOHOL TEMPERANCE IN HEALTH AND DISEASE

ABSTRACT

There is hardly a disagreement about the dangers of alcoholism ranging from addiction through cardiovascular disorders and cancers to death. But there seem to be conflicting science and sense on the effect of low to moderate intake of alcohol and abstinence in health and disease. Some earlier scientific reports maintain that moderate intake of alcoholic beverages is beneficial to health; seemingly more beneficial than total abstinence from imbibing in the habit. A number of researchers went further to classify the different forms of alcoholic beverages and their effect on health at moderate intake. There exists a near general agreement on the health benefit of taking red wine in moderation; which was attributed to bioflavonoids and antioxidants used in the preparation of red wine and not the alcoholic medium of delivery. This logically suggests that these antioxidants can elicit the same benefit as supplements without alcohol. Individual variations are seen to exist in alcohol intake and handling; and genes can also act differently in people of different races and genders, further influencing whether someone is predisposed to addiction. This review appraises some scientific reports on the intake of alcoholic beverages, with emphasis on low to moderate levels, from limitless resource in all accessible internet databases.

Keywords: Alcohol Handling;Reward; Addiction; Dopamine.

1.0 INTRODUCTION

Drinking alcohol has been associated with a myriad of health challenges but these are often attributed to overindulgence (World Health Organization, 2009). Claims have been made that a life devoid of alcohol does not have optimal health. Many chemicals are classified as "alcohol" but ethyl alcohol (also known as ethanol) is the only safely consumable form of alcohol (American Academy of Paediatrics, 2015).) "Ethanol is the type of alcohol found in alcoholic beverages and is also used in scents, flavourings, colourings and drug formulations. Features of drinking alcoholic beverages include euphoria, impaired thought processes and decreased mechanical efficiency. Alcohol has over the years been an accepted part of the human diet and is the intoxicating component of beverages such as palm wine, whiskey and beer. It occurs naturally from the palm tree as palm wine but is mostly derived as a product of the fermentation of various types of sugars found in food and drinks. Ethyl alcohol is one of the most widely used and most commonly abused drugs in the world. It is used orally and is absorbed by the mucosa of the stomach and the small intestine. 90% of consumed alcohol is metabolized in the liver, while the remaining 10% is excreted unchanged by the kidneys and lungs" (Dubowski K.M., 1985).

1.1 Starting to drink alcohol

Starting to drink alcohol is influenced by environment, culture, tradition and upbringing. Peer influence and belief in people of value enhance our inclination to copy their habits, including drinking alcohol; as perceptions are easily influenced by status. Preconceptions around the

elderly or people of status and prestige are important because we're likely to overvalue things related to them and assign too low a value to things not related to them. When people that we idolize are in the habit of drinking alcohol, we are drawn to do same in desperate hopes of impressing them; thus, decisions are made to try out alcoholic drinks even when they are not offered. In such environment people that do not drink alcohol are considered unconventional and social misfits. The tasting and starting off with alcohol imply a person's first few experiences with alcoholic beverages, no matter at what age this happens. Research has shown that if a person starts to drink alcohol in the early teenage years, they will be more likely to run into alcohol problems later in life and this can also impair both physical and emotional development (National Research Council (US) and Institute of Medicine (US) Committee on Developing a Strategy to Reduce and Prevent Underage Drinking, 2004). Teenagers have "spurts of physical growth in their body, while adolescence is also a time for huge development mentally, emotionally and psychologically" (http://www.drugs.ie/). If alcohol becomes something that serves as an expedient during adolescence, it can impair that development and make them more susceptible to addiction and chronic effects (Moss HB, Kirisci L, Gordon H.W., Tarter.E., 1994). This suggests that postponing the onset of association with alcoholic beverages might minimise the attendant dependence and addiction with consequent social and physiological ills associated with it.

1.2 Alcohol handling

"After oral absorption, alcohol is absorbed almost completely from the duodenum, primarily by diffusion at an extremely variable rate which depends on several factors that include; the rate of drinking, food, gastric metabolism, volume, type and alcohol concentration of the beverage" (Dubowski K.M., 1985). "The amount, timing and type of food all have an effect. The effect of

food on alcohol is primarily due to the delay in gastric emptying seen after meal consumption" (Rall T., 1990). "Less concentrated alcoholic solutions are absorbed more slowly, and the faster the rate of drinking, the faster the absorption. Also, gastric metabolism, as well as hepatic first-pass metabolism can significantly decrease the bioavailability of alcohol and thus the amount of alcohol getting into the systemic circulation" (Rall T., 1990).

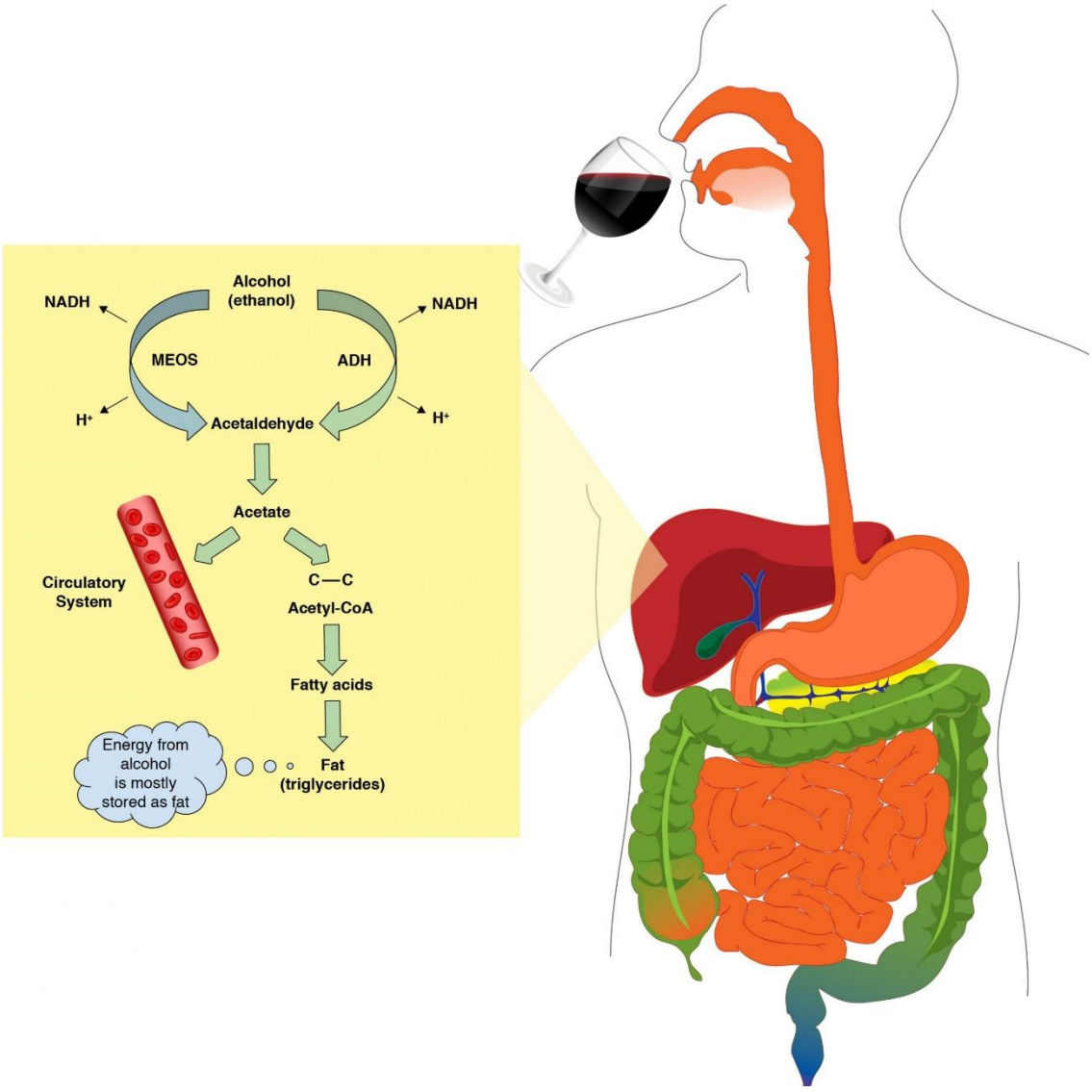

Figure 1: Ethanol Metabolism

1.3 Variability in alcohol handling

There is ethnic, age, genetic and gender variations to the effect of alcohol on the body. The role of region and race/ethnicity in alcohol consumption among older adults has been reported (Wilson JR, McClearn GE, Johnson RC., 1978). Differences in the metabolizing enzymes ensure that alcohol is handled differently by persons of different races (Jorgenson, E. et al., 2017). Most of the time, women are more prone to the toxic effects of alcohol than men, because they have smaller body size and the distribution of alcohol is into total body water. Women are known to have lower proportion of total body water compared to men, even if they have the same weight (Holford N.H.G., 1987). "Older adults are also more sensitive to the intoxicating effects of alcohol because they metabolize alcohol more slowly" (Rigler S.K., 2000). "Males and females differ in their ability to metabolize alcohol. The main biological differences between men and women concerning alcohol consumption are attributed to several contributing factors involved including heredity and genetics" (http://www.pbinstitute.com/). "This difference is partly due to variations in the amount and activity of alcohol dehydrogenase (ADH), the enzyme responsible for metabolizing alcohol. In general, males metabolize alcohol more efficiently than females because they have ADH in the stomach and very active ADH in the liver. Females do not express ADH proteins in their stomachs and the ADH in their livers is not as efficient" (https://sites.duke.edu/). "Gender differences in alcohol metabolism result in increased blood alcohol concentration for females compared to males if they both consume the same amount of alcohol. For the same number of drinks, it is easier for females to become intoxicated" (https://sites.duke.edu/). It is also "suggested that females are more susceptible than males to alcohol-induced liver inflammation, cardiovascular disease, memory blackouts, hangovers, and certain cancers" (http://www.issup.net/).

Variations in alcohol handling can also be partially caused by heredity when the disease runs in the family. “However, this does not necessarily mean that an alcoholic parent will pass the disease onto a child. It simply means that there could be specific risk factors involved” (http://www.pbinstitute.com/). “Genes might play a direct role in the development of alcoholism, as in affecting the body's metabolism of alcohol; or they might play a less direct role, influencing a person's temperament or personality in such a way that the person becomes vulnerable to alcoholism. Those with a history of alcoholism in their family have the highest risk of becoming alcoholics” (National Institute on Alcohol Abuse and Alcoholism, 2008). With multiple relatives with alcohol addictions or other substance use disorders, one may have inherited the genes that exposes to alcoholism. The more family members one has with an alcohol problem, the higher the risk of becoming alcoholic. “Many independent lines of evidence point to genetic contributions to its etiology. Adoption studies show that alcoholism in adoptees correlates more strongly with their biological parents than their adoptive parents” (Heath AC, 1995; Sigvardsson S, Bohman M, Cloninger CR., 1996; Cloninger CR, Bohman M, Sigvardsson S., 1981; Bohman M, Sigvardsson S, Cloninger CR., 1981). “Twin studies in the US and Europe suggest that approximately 45-65% of the liability is due to genetic factors” (Heath AC, et al. 1997; Prescott CA, Kendler KS. 1999; Kendler KS, Neale MC, Heath AC, Kessler RC, Eaves LJ.,1994; Pickens RW, et al., 1991). “Animal studies also demonstrate genetic liability; mice and rats have been selectively bred for many traits associated with alcohol dependence, including alcohol preference, alcohol sensitivity, and withdrawal sensitivity” (McBride WJ, Li TK., 1998). “Genetic factors affect the risk not only for alcohol dependence, but also the level of alcohol consumption and the risk for alcohol-associated diseases, including cirrhosis and upper gastrointestinal cancers” (Foroud T, Edenberg HJ, Crabbe JC., 2010). It should be emphasized

that while genetic differences affect risk, there is no “gene for alcoholism,” and both environmental and social factors weigh heavily on the outcome.

1.4 Habit forming potential of alcohol

Through evolutionary trends living beings are compelled to repeat habits that are desirable as this promotes survival. Such habits as eating food and sexual intercourse bring bursts of pleasure to ensure nourishment and procreation which are vital elements of survival (Kalivas PW, Volkow ND, 2005). “The brain strengthens the connections that allow this rewarding behavior to occur” and it is then easier to do next time (Nutt D., 1999). But the body makes adjustments for consumption habits and includes having to need more quantity to reach the same level of satiety (Kalant H., 1998). Subsequently the organism finds it increasingly difficult to function “normally” without topping up with the habit. If this source of joy is suddenly withdrawn it leads to often violent emotional, psychological and physiological reactions (Schuckit M.A.,1995). Thus, the journey from consumption through tolerance and dependence to addiction ends with withdrawal reactions on the path of recovery. Alcohol consumption initially leads to euphoria because it releases dopamine (DA) into the “reward center” of the brain. But after drinking a lot for a long time, the dopamine is no longer released leading to dysphoria (Koob GF, Nestler E.J. 1997). The dopamine system originates in the ventral tegmental area (VTA) and connects to the nucleus accumbens, prefrontal cortex as well as hippocampus. This is the mesocorticolimbic system. “Natural activities such as eating, drinking, and sex activate the nucleus accumbens, inducing considerable communication among this structure's neurons” (http://www.ncbi.nlm.nih.gov/). The resultant effect of this essential connection is the release of dopamine (Koob GF, Nestler E.J. 1997). “An optimally functional nucleus accumbens cause normal, consistent and predictable communication among its neurons. When an electrical signal

within a stimulated neuron reaches the synapse with the target neuron it triggers the release of dopamine into the synapse" (http://www.ncbi.nlm.nih.gov/). "The dopamine travels across the synaptic gap until it reaches the target neuron at which time it binds to the postsynaptic neuron's dopamine-specific receptors, which in turn has an excitatory effect that generates an internal electrical signal within this neuron" (http://www.ncbi.nlm.nih.gov/). "However, not all of the released dopamine binds to the target neuron's receptors. Extra dopamine may be chemically deactivated, or it may be quickly reabsorbed by the releasing neuron through a system called the dopamine reuptake transporter" (http://www.knowingneurons.com). "As soon as the extra dopamine has been deactivated or reabsorbed, the two cells are "reset," with the releasing neuron prepared to send another chemical signal and the target neuron prepared to receive it. The released dopamine brings about feelings of pleasure and elation. As dopamine levels lessen, so do the feelings of pleasure. A repetition of the activity will lead to further release of dopamine and consequent feelings of pleasure and euphoria. Thus, the pleasurable feelings obtained from dopamine release positively reinforce such activities and motivate the repeating of these actions" (Koob GF, Nestler E.J. 1997). "Alcohol mostly affect the brain by increasing release of the neurotransmitter GABA, which causes an overall "depressive" effect on brain activity, including retarded and impaired thought processes, movement, and reaction time" (Mihic SJ, Harris R.A., 1997).

"Because alcohol is a depressant, this can negatively affect the brain in the long run, causing more stress, anxiety, and sadness than before. An area of the brain called the neostriatum is involved in the brain's reward system" (Koob GF, Nestler E.J. 1997). "When alcohol activates the reward pathway, causing the cells to increase the amount of dopamine in the area the brain compensates for these sudden changes by reducing the number of cells that can respond to

dopamine, so that the next time a drug is used, the effect is not as strong" (Koob GF, Nestler E.J. 1997). "Unfortunately, this also causes the user to increase drug use in order to get that same "high," a term called "tolerance"; the phenomenon of decreased effect with prolonged exposure to a drug" (Kalant H.,1998). "When the tolerance occurs with a single exposure to the drug it is called acute tolerance. Chronic tolerance occurs over repeated uses of the drug. Tolerance to alcohol can be metabolic (pharmacokinetic) - due to induction of enzymes or pharmacodynamic - due to physiological adaptation of the body to its presence" (Visovsky, C., Zambroski, C., Hosler, S. and Workman, L., 2019). As the brain continues to adapt to alcohol, the regions of the brain responsible for judgment and memory are also changed. This makes alcohol-seeking behaviour a habit, and the user becomes dependent on it and ultimately addicted to the drug.

1.5 Regulatory attempts on the use of alcohol

The health challenges from the social use of alcoholic beverages are noticeably huge both for the individual and society and thus attempts have been made to curtail it (Cox, E., Wells, C. & Campbell C., 2014). "In the U.S.A., the National Prohibition of Alcohol (1920-33) was undertaken to reduce crime and corruption, solve social problems, reduce the tax burden created by prisons and poorhouses, and improve health and hygiene in America by eliminating alcohol intake" (Oliver Richardson. "Wine marketing: modelling the ethics of the wine industry using qualitative data", Qualitative Market Research: An International Journal, 2005). The lure of alcohol and the deep root it has taken on society ensured that it turned out a miserable failure on all counts (Mark Thornton). High taxation is imposed on alcoholic substances but this has not discouraged the consumption noticeably. Many countries and religions also placed bans on the dealing and intake of alcohol without been able to eradicate it (King D., 2014). These are a reflection of the force

of addiction to alcohol and its acceptance by different rational societies that find it impossible to reduce the burden of indulgence on alcoholic beverages.

2.0 HOW MUCH ALCOHOL IS TOO MUCH?

"To reduce the risk of alcohol-related harms, the recommended low risk weekly guidelines for adults are: less than 11 standard drinks (approx. 110g of alcohol) in a week for women, and less than 17 standard drinks (approx. 170g of alcohol) in a week for men" (Rose, M. E.; Grant, J. E. 2010 and USDA 2020). Binge drinking - the consumption of high quantities of alcohol (≥4/5 drinks for women/men) within a time period of 2 h (NIAAA, 2004) or heavy episodic drinking, comes with acute and chronic consequences (Esser MB, Hedden SL, Kanny D, Brewer RD, Gfroerer JC, Naimi TS., 2011) and is not covered by this guideline. This Guideline does not recommend that individuals who do not drink alcohol start drinking for any reason and that if adults of legal drinking age choose to drink alcoholic beverages, drinking less is better for health than drinking more. "It also notes that some persons; that are pregnant or might be pregnant, under the legal age for drinking, recovering from an alcohol use disorder or have certain medical conditions or are taking certain medications that can interact with alcohol should not drink alcohol at all. Not drinking alcohol also is the safest option for women who are lactating" (USDA, 2020). "Alcohol intake inhibits the milk ejection reflex, causing a temporary decrease in milk yield" **(**onlinelibrary.wiley.com**)**. "The alcohol concentrations in breast milk closely resemble those in maternal blood. The amount of alcohol presented to nursing infants through breast milk is approximately 5-6% of the weight-adjusted maternal dose, and even in a theoretical case of binge drinking, the children would not be subjected to clinically relevant amounts of alcohol. Newborns metabolize alcohol at approximately half the rate of adults" (Maija Bruun Haastrup, Anton Pottegård and Per Damkier, 2014).

3.0 MODERATE ALCOHOL CONSUMPTION

"Drinking alcohol even within the recommended limits has been found to increase risk for cancer, and for some types of cancer, the risk increases even at low levels of alcohol consumption" (Rose, M. E.; Grant, J. E., 2010). Consumption of alcoholic beverages within reasonable or average limits; not excessive or extreme, has been attributed to positive outcomes (Holahan, C. J., Schutte, K. K., Brennan, P. L., Holahan, C. K., Moos, B. S. & Moos, R. H., 2010; Heather Saul, 2013). Research found that people who drank heavily had a lower mortality rate than those who did not drink any alcohol at all Holahan, C. J., Schutte, K. K., Brennan, P. L., Holahan, C. K., Moos, B. S. & Moos, R. H., 2010; Heather Saul, 2013; Chikritzhs T, Fillmore K, Stockwell T. A., 2009). "But although past studies have indicated that moderate alcohol consumption has protective health benefits (e.g., reducing risk of heart disease), more recent studies show this may not be true" (Andréasson S, Chikritzhs T, Dangardt F, Holder H, Naimi T, Stockwell T., *2014*; Knott CS, Coombs N, Stamatakis E, Biddulph JP (2015). "While some studies have found improved health outcomes among moderate drinkers, it's impossible to conclude whether these improved outcomes are due to moderate alcohol consumption or other differences in behaviours or genetics between people who drink moderately and people who do not" (Holmes MV, Dale CE, Zuccolo L, et al (2014); Naimi TS, Brown DW, Brewer RD, et al (2005); Rosoff DB, Davey Smith G, Mehta N, Clarke TK, Lohoff FW (2020), Mukamal, K. J., Jensen, M. K., Gronbaek, M., Stampfer, M. J., Manson, J. E., Pischon, T. & Rimm, E. B. (2005);). Low levels of alcohol consumption can increase high density lipoprotein cholesterol (Collins, M. A., Neafsey, E. J., Mukamal, K. J., Gray, M. O., Parks, D. A., Das, D. K. & Korthuis, R. J., 2009). while facilitating blood circulation and decreasing inflammation (Collins, M. A., Neafsey, E. J., Mukamal, K. J., Gray, M. O., Parks, D. A., Das, D. K. & Korthuis, R. J.,

2009). Inflammation is strongly implicated in the severity and progression of diseases like Alzheimer's (Collins, M. A., Neafsey, E. J., Wang, K., Achille, N. J., Mitchell, R. M. & Sivaswamy, S., 2010), and experiments on isolated neurons "suggest that small amounts of alcohol can precondition brain cells to deal with stressful conditions". This helps to suppress inflammation and prevent cognitive deterioration (Collins, M. A., Neafsey, E. J., Wang, K., Achille, N. J., Mitchell, R. M. & Sivaswamy, S., 2010; Lindsay, J., Laurin, D., Verreault, R., Hebert, R., Helliwell, B., Hill, G. B. & McDowell, I., 2002). "Although several studies pointed out that drinking low-to-moderate amounts of any form of alcohol may reduce the risk of developing Alzheimer's disease, others suggest that red wine has the highest potential to prevent or delay cognitive decline" (Larrieu, S., Letenneur, L., Helmer, C., Dartigues, J. F. & Barberger-Gateau, P., 2004; Luchsinger, J. A., Tang, M. X., Siddiqui, M., Shea, S. & Mayeux, R., 2004). For example, one study regularly tested over 5000 older adults on learning, memory and attention tasks for seven years (http://www.alzdiscovery.org/). Those who drank red wine did better in each tested class and presented slower age-related cognitive decline as likened to those who drank other forms of alcohol (Arntzen, K. A., Schirmer, H., Wilsgaard, T. & Mathiesen, E. B. 2010). "Red wine contains other compounds besides alcohol, including the antioxidant resveratrol, which may have potential benefits for human health" (http://www.alzdiscovery.org/). But the amount of resveratrol in red wine is so low that it is probably not relevant to human health (Arntzen, K. A., Schirmer, H., Wilsgaard, T. & Mathiesen, E. B. 2010). However, it is necessary to separate the effects of red wine from other factors. For example, people who drink wine have a tendency or disposition to buy healthier foods (Johansen, D., Friis, K., Skovenborg, E. & Gronbaek, M., 2006), are generally better-educated (Klatsky, A. L., Armstrong, M. A. & Kipp, H., 1990), exercise more and maintain a

healthier body mass (Barefoot, J. C., Gronbaek, M., Feaganes, J. R., McPherson, R. S., Williams, R. B. & Siegler, I. C.; 2002). All these are factors that are also associated with a lower risk of developing Alzheimer's disease. Drinking red wine may then be associated with persons who are more likely to also choose healthier lifestyles. "Drinking at levels above the moderate drinking guidelines significantly increases the risk of short-term harms, such as injuries, as well as the risk of long-term chronic health problems, such as some types of cancer" (Paschall, M. & Lipton, R. I., 2005; Vinson DC, Maclure M, Reidinger C, Smith GS (2003; Nelson DE, Jarman DW, Rehm J, et al., 2013). "Some investigators have proposed that cognitive performance worsens in direct proportion to the severity and duration of alcoholism" (Parsons, O.A.,1998; Beatty, W.W., Tivis, R., Stott, H.D, Nixon, S.J. and Parsons, O.A., 2000). "Studies suggest that social drinkers who consume more than 21 drinks per week also fit into this category" (pubs.niaaa.nih.gov). "Other investigators have suggested that cognitive deficits may be detectable only in those alcoholics who have been drinking regularly for 10 years or more" (Beatty, W.W., Tivis, R., Stott, H.D, Nixon, S.J. and Parsons, O.A., 2000). "Long-term, light-to-moderate social drinkers have been found to fall into this category as well, showing cognitive deficits equivalent to those found in detoxified alcoholics" (Parsons, O.A., and Nixon, S.J., 1998; Eckardt, M.J.; File, S.E.; Gessa, G.L.; et al., 1998).

According to one centenarian, the key to longevity is regular drinking (Gillian Fuller, 2015). "During her milestone 100th birthday celebration, Pennsylvania-based Pauline Spagnola said that her secret for living a long life is alcohol. Strangely enough, Spagnola isn't the first to credit booze for her long life. Back in 2013, a 101-year-old Staten Island woman insisted the same, claiming she drank two glasses of wine, a glass of Southern Comfort and one beer each day" (Gillian Fuller, 2015). It can be reasoned that the alcohol is not the total enabler but that the

people who use moderate to low alcohol levels share other characteristics that make them less likely to experience both cognitive decline and other degenerative diseases. For example, perhaps these people are more likely to have an active social life and maintain time-tested practices that are essential for living a long, healthy life like exercising and eating right.

4.0 COMPULSIVE DRINKING AND ALCOHOL USE DISORDER

"Alcohol consumption is associated with a variety of short- and long-term health risks, including motor vehicle crashes, violence, sexual risk behaviours, high blood pressure, and various cancers" (Di Castelnuovo A, Costanzo S, Bagnardi V, Donati M, Iacoviello L. and de Gaetano G., 2006). The risk of these harms increases with the amount of alcohol consumed (Di Castelnuovo A, Costanzo S, Bagnardi V, Donati M, Iacoviello L. and de Gaetano G., 2006). "For some conditions, like some cancers, the risk increases even at very low levels of alcohol consumption" (Rehm J, Shield K., 2014). The popular byword "First the man takes a drink, and the drink takes another drink, then the drink takes the man" or paraphrased as "First you take a drink, then the drink takes another drink, then the drink takes you" summarized the acceptance that voluntariness in taking alcohol ends with the first drink; at least for many persons. The addictive potential and lure of alcohol is such that many a person has been programmed by genetic and other disposition to remain in its hook once exposed. For some persons who feel that they can control their alcoholic intake end up being controlled by the alcohol. In this master-servant relationship, the roles are programmed to change. Compulsive drinking usually ends up with alcohol use disorder and may be due to dysfunction in a specific brain pathway that normally regulate drinking. The results as reported in the journal Biological Psychiatry point to that direction (Lindsay R. Halladay, Adrina Kocharian, Patrick T. Piantadosi, Michael E.

Authement, Abby G. Lieberman, Nathen A. Spitz, et. al., 2019). Alcoholism also called alcohol use disorders can be beguiling but harmful, and often there is no clear line between alcohol abuse and alcohol dependence. Eventually alcohol dominates thinking, emotions, and actions and becomes the primary means through which a person can deal with people, work, and life. The Impact of Alcoholism affects the individual, the family and the society at large. For the individual alcohol is responsible for a myriad of physical health challenges involving almost all the organs of the body.

4.1 Brain function

Alcohol acts as a general central nervous system depressant, but it also affects specific areas of the brain to a greater extent than others. It can damage memory and brain function and after only a few drinks memory can be impaired and brain processes slow down. Larger quantities of alcohol can lead to short-term memory failure or 'blackouts' (White A., 2003). "Drinking heavily over a long period of time can also have long-term effects on memory. Alcohol affects many parts of the brain and the most prevalent alcohol-associated brain impairments affect visuospatial abilities and higher cognitive functioning" (Oscar-Berman, M.; Shagrin, B.; Evert, D.L.; and Epstein, C.,1997). "Visuospatial abilities include perceiving and remembering the relative locations of objects in 2- and 3-dimensional space. Examples include driving a car or assembling a piece of furniture based on instructions contained in a line drawing. Higher cognitive functioning includes the abstract-thinking capabilities needed to organize a plan, set it in motion, and change it as needed" (Giancola, P.R., and Moss, H.B., 1998). "With long-term heavy drinking, recalling old memories and laying down new ones can become more difficult. Alcohol-related dementia (ARD) is a form of dementia caused by long-term, excessive drinking,

resulting in neurological damage and impaired mental processing. Epidemiological studies show an association between long-term alcohol intoxication and dementia" (Elena Lobo; Carole Dufouil; Guillermo Marcos; Bernardo Quetglas; Pedro Saz; Eliseo Guallar; Antonio Lobo, 2010). This study did not support the hypothesis that low-to-moderate alcohol consumption prevents cognitive decline. "Alcohol can damage the brain directly as a neurotoxin, or it can damage it indirectly by causing malnutrition, primarily a loss of thiamine" (vitamin B1) (research.omicsgroup.org).

"The human brain is still in the process of development until the age of 18 or 19, and it may be more susceptible to damage than the adult brain. In adolescents who regularly drink alcohol, parts of the brain important in planning and emotional control have been found to be smaller than expected. Alcohol use by students is a major public health problem, leading to decrease in academic performance, injuries, blackouts, alcohol dependence and other maladies" (Menizibeya Welcome Osain and Vladimir Pereverzev Alekseevic, 2010). "This study shows that alcohol use even in moderate doses leads to decrease in academic performance. Negative effect of alcohol use on intellectual activities of students using academic performance as a criterion increases with increase in time and dose of alcoholic drinks" (Menizibeya Welcome Osain and Vladimir Pereverzev Alekseevic, 2010).

4.2 Carcinogenicity

In 1931, Otto Heinrich Warburg (1883-1970) was awarded the Nobel Prize for his thesis: "The Primary Cause and Prevention of Cancer." He stated that cancer is the result of an anti-physiological diet and lifestyle (http://www.familyhom.euni.org/). "The lack of oxygen and acidosis are two sides of the same coin: if you have one, you have the other" (Otto Warburg, Franz Wind, and Erwin Negelein, 1927). Basic chemistry explains that alkali solutions (pH

greater than 7.0) tend to absorb oxygen while acids (pH below 7.0) tend to expel oxygen. A weak alkali can absorb much more oxygen ($O_{2)}$ than a weak acid. Therefore, when the body becomes acidic by dropping below pH7.0, oxygen is driven out of the body, thereby inducing cancer. According to Warburg: "All normal cells must have oxygen, but cancer cells can live without oxygen—a rule without exception. “In summary, cancer occurs in the absence of free oxygen in the body, and therefore whatever can deprive the body of oxygen can cause cancer to manifest” (Koppenol, W., Bounds P. and Dang, C., 2011). All body fluids, except for stomach and urine are supposed to be mildly alkaline at pH7.4. Stomach fluids must remain acidic to digest food and urine must remain acidic to remove wastes from the body. Blood is the exception. Blood must remain at an alkaline pH7.4 to retain its oxygen. Alcohol causes a depletion of some minerals in the body. When insufficient mineral is in the diet, the body is forced to remove minerals from other body fluids (saliva, spinal fluid, kidney, liver etc) in order to maintain the blood pH at 7.4. This causes the demineralized fluids and organs to become acidic and therefore anaerobic, thus inducing not only cancer, but a host of other degenerative diseases including cardiovascular disorders, diabetes and arthritis. Drinking alcohol can also increase the risk of multiple types of cancer due partly because the body breaks down alcohol into acetaldehyde, a chemical that damages DNA (Cunningham FH, Fiebelkorn S, Johnson M, Meredith C., 2011). Damaged DNA can lead to cancer cells and tumours (Kastan M.B., 2008).

4.3 Cardiovascular and other disorders

Alcohol has been implicated in several cardiovascular disorders like hypertension, arteriosclerosis and stroke. Alcohol can cause a long-term increase in blood pressure and people with high blood pressure face a variety of health risks, including heart disease, heart attack, and stroke (Holmes MV, Dale CE, Zuccolo L, et al., 2014; Naimi TS, Brown DW, Brewer RD, et al.,

2005; Rosoff DB, Davey Smith G, Mehta N, Clarke TK, Lohoff FW.,2020; Mukamal, K. J., Jensen, M. K., Gronbaek, M., Stampfer, M. J., Manson, J. E., Pischon, T. & Rimm, E. B., 2005). Constant intake of alcohol can lead to mineral deficiency in the blood which will subsequently result in acidosis (Otto Warburg, Franz Wind, and Erwin Negelein, 1927; Koppenol, W., Bounds P. and Dang, C., 2011). "The artery which conveys blood from the heart to other parts of the body is essentially the same as the vein, which returns blood to the heart. The major difference is that the artery surface is made up of muscle tissue that can squeeze and compress the artery, resulting in an increased blood pressure, thereby ensuring the blood gets to the distant parts of the body. This is muscle tissue that is most amenable to disintegration by lactic acid. Intake of alcohol leads to increased acidity of the blood. Once the body's fluids become acidic, the muscle tissue surface of the arteries become a susceptible target. With the muscle tissue disintegrated, the remainder of the artery wall is weakened. As the wall is thin, it is exposed to the very positively charged external acids (acids are positively charged and alkali are negatively charged). This causes various negatively charged components in the blood such as phospholipids to be attracted and stick to the positive acid weakened wall. A host of other components like collagen, fibrin, triglycerides, heavy metals, proteins, mucopolysaccharides, muscle tissue and debris plus Low-density lipoprotein cholesterol attach themselves to the phospholipids anchored on the weakened artery wall. All of this form a plaque bound together by calcium. This results in a stronger, thickened and hardened artery wall which diminishes the size of the opening in the artery-arteriosclerosis. Thus, the arteriosclerosis, heart attack and stroke were caused by inflammation of the blood vessel walls due to acidosis which was a result of mineral deficiency caused by constant intake of alcohol" (Otto Warburg, Franz Wind, and Erwin Negelein, 1927). Alcoholics usually have inadequate content of significant nutrients. Deficiencies in vitamin B

pose health risks in people with alcoholism. Other vitamin and mineral deficiencies, however, can also cause numerous health problems. Alcohol interference in folate metabolism can cause severe anemia. Wernicke-Korsakoff syndrome often manifest from severe thiamine (vitamin B1) deficiency in alcoholism. Symptoms of this syndrome include severe loss of balance, confusion, and memory loss. Eventually, it can result in permanent brain damage and death. Also, Vitamin B12 deficiencies can also lead to pain, tingling, and other abnormal sensations in the arms and legs; a condition peripheral neuropathy.

5.0 SOCIOECONOMIC EFFECT OF ALCOHOL ABUSE

The general impact of alcohol abuse extends far beyond the financial costs to family life and the society (Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer R.D., 2015). "Alcohol use results in Fatigue, impaired mental alertness, attention deficit, decreased work and academic performance. The alcoholic problem of a family member would have impact on both the nuclear and extended family. This rubs off on the community, schools, the workplace, the healthcare system and the entire society. The social impact of alcohol abuse is a separate issue from the financial costs involved, and that impact begins in the home, extends into the community, and consequently affects society as a whole, much like the financial impact does. Research on the effects of alcohol abuse on families shows that alcohol abuse and addiction play a role in intimate partner violence, causes families' financial problems, impairs decision-making skills, and plays a role in child neglect and abuse" (Lander L, Howsare J, Byrne M., 2013). "As with the financial costs of alcohol abuse, studies have found occasional binge drinking can affect families also. Research suggests that the risk of intimate partner violence rises not only in the

context of frequent drinking, but also when a partner has consumed a large volume of drinks in one sitting" (Wilson IM, Graham K, Taft A., 2014).

5.1 Alcohol Abuse and Children

"Fetal alcohol syndrome (FAS) is one of the most common direct consequences of parental alcohol use in the United States, caused by alcohol consumption by the mother during pregnancy" (http://www.verywellmind.com/). Children with FAS display a variety of symptoms, many of which are lifelong and permanent. Children who grow up in a home with a loved one dealing with alcohol addiction may be affected as well; they are at significant risk to develop alcohol use disorders themselves. "Growing up in a home where at least one parent has an alcohol use disorder can increase a child's chances of developing psychological and emotional problems" (http://www.verywellmind.com/).

7.2 Alcoholic abuse and prostitution

Alcohol use decreases inhibition and increases the inclination to risky sexual behaviour (Silbert MH, Pines AM, Lynch T., 1982). "The existence of a relationship between substance abuse and prostitution in and of itself does not imply causality" (pubmed.ncbi.nlm.nih.gov). "It is not clear whether substance abuse is one of the factors that pushed these women into prostitution or whether it was prostitution that caused their drug involvement. Most likely, both prostitution and substance abuse are the behavioural translations of these women's endless cycles of victimization and severely disturbed backgrounds, as well as an expression of the self-destructive pull, the sense of hopelessness, helplessness, negative self-concept and psychological paralysis reported by almost every subject in the study" (Ugeskr Laeger, 2004).

6.0 ABSTINENCE IN HEALTH AND DISEASE

"Abstaining from alcoholism or teetotalism is the practice and promotion of complete abstinence from alcoholic beverages. The word abstinence refers to voluntary prevention of oneself from indulging in bodily activities that provide pleasure and are potentially addictive; like sexual intercourse, alcohol or food" (https://www.news-medical.net/health/What-is-Abstinence.aspx). "Abstinence can be due to personal preferences, religious practices of practical considerations. In medicine abstinence also refers to discontinuation of an addictive substance. This may lead to intense craving for the drug or withdrawal syndromes" (https://www.news-medical.net/health/What-is-Abstinence.aspx.). "Abstinence may be a temporary or short-term goal meant for short durations of time. This includes refraining from compulsive drinking" (https://www.news-medical.net/health/What-is-Abstinence.aspx.). The time and the measure are voluntary and thus meant to enhance life. This is different from psychological mechanism of repression where the abstinence is not willingly adopted. Abstaining from alcohol can lead to several health benefits and this is more noticeable for former addicts to alcohol (Fernandez DP, Kuss DJ, Griffiths M.D., 2020). This has made it trendy for many persons who are seeking to make healthy life changes to desire to quit drinking alcoholic beverages completely. The brain, cardiovascular and other systems show considerable improved functioning in the absence of alcohol (Fernandez DP, Kuss DJ, Griffiths M.D., 2020). No advantages have been convincingly proven to the contrary.

6.1 Benefits for the brain

Addiction to alcohol leads to decreased mental alertness, slower reaction time and serious depression among a wide array of ills. The consequence of this can be seen in slurred speech and stumbling movements. This can lead to difficulty in handling previously ordinary tasks like

driving or operating machinery. Structural imaging studies reveal that compared with non-alcoholics', most alcoholics' brains are smaller and less dense (Pfefferbaum, A.; Rosenbloom, M.; Crusan, K.; and Jernigan, T.L., 1988; Pfefferbaum, A.; Lim, K.O.; Zipursky, R.B et al., 1992). Loss of brain volume is most noticeable in two areas: the outer layer (i.e., the cortex) of the frontal lobe, which is considered a major centre of higher mental functions (Pfefferbaum, A.; Lim, K.O.; Zipursky, R.B et al., 1992) and the cerebellum, which is responsible largely for gait and balance as well as certain aspects of learning (Lyvers, M., 2000). Support for these results is provided by functional imaging studies, which reveal altered brain activity throughout the cortex and cerebellum of heavy drinkers (Sullivan, E.V.; Rosenbloom, M.J., 1995; Eberling, J.L., and Jagust, W.J., 1995). In addition, functional imaging often is sufficiently sensitive to detect these irregularities before they can be observed by structural imaging techniques, and even before major cognitive problems themselves become manifest (Eberling, J.L., and Jagust, W.J., 1995).

6.2 Benefits for the liver

Drinking alcoholic beverages over task the liver as it is not processed by the body the same way that other things are processed in the liver. The rate of oxidation of alcohol is constant and does not change with concentration. For an average man this is approximately 12.5ml/hour and is proportional to body weight (Holford N.H.G., 1987). Alcohol can take several days to get through the liver, depending on rate and quantity consumed (Holford N.H.G., 1987). This gradually leads the alcoholic to a fatty liver, liver scarring and other liver disease which are life threatening. The liver is an extremely important organ in maintaining health and adequate body function. Total abstinence from alcohol is the only protection from alcohol-related liver disease (ARLD). Alcohol abstinence can prevent liver damage from progressing and reverse the damage that has been caused by years of excessive drinking. On alcohol abstinence the liver begins to

repair itself. Alcoholic fatty liver, liver scarring and other life-threatening liver disease can gradually go back to a healthier state. This depends on factors which include length of time spent drinking, age and lifestyle.

6.3 Other health benefits of alcohol abstinence

Not only will alcohol abstinence significantly benefit the brain and liver, but it will also decrease risk of cancers, cardiovascular and other diseases. Drinking alcohol can increase the risk of multiple types of cancer (Nelson DE, Jarman DW, Rehm J, et al., 2013; Di Castelnuovo A, Costanzo S, Bagnardi V, Donati M, Iacoviello L, de Gaetano G., 2006; Rehm J, Shield K., 2014; Kastan M.B., 2008), thus, abstainers from alcohol face a much lower risk of cancer than people who drink. Complete abstinence from alcohol helps maintain a healthy blood pressure. Alcohol decreases immunity which increases susceptibility to disease (Di Castelnuovo A, Costanzo S, Bagnardi V, Donati M, Iacoviello L, de Gaetano G., 2006). People who drink tends to experience more colds, flus, and other illnesses than people who don't drink. That's because alcohol intake weakens the immune system. Even a moderate amount of alcohol can suppress the immune system and increase susceptibility to illness. Abstinence from alcohol thus leads to a stronger immune system and this aids protection from many ailments.

A good night's sleep is extremely important to anyone's health. Alcohol disrupts the circadian rhythm, an internal process that helps control sleep-wake cycle. More specifically, the drug prevents one from getting enough deep sleep leading to frequent wakefulness throughout the night and exhaustion the next day (Chakravorty S, Chaudhary NS, Brower K.J., 2016; de Zambotti M, Willoughby AR, Baker FC, et al., 2015). Quitting drinking leads to improved sleeping habits. Alcohol dehydrates the body which will affect skin tone and complexion

(https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/alcohol-facts-and-statistics). Abstinence leads to better hydration of the skin making it to look healthier. Each drink of Alcohol increases intake of empty calorie that fills the body with excess fat, thus with abstinence, there is likely to be loss of weight and increased energy (https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/alcohol-facts-and-statistics). Moderate alcohol consumption is claimed to help protect the hearts of adults with type 2 diabetes. Heavy drinking, however, is associated with obesity, which is a risk factor for this form of diabetes. In addition, alcohol can cause hypoglycaemia, a drop in blood sugar, which is especially dangerous for people with diabetes who are taking insulin.

7.0 ALCOHOL RECOVERY

Because changes associated with the use of alcohol can be damaging to the body system, efforts are made to put the alcoholic on a path to recovery. Recovery from the effect of alcohol abuse can only commence with an understanding of the harmful effect and willingness to choose healthier life style. Quitting drinking will pave the way for the body to heal itself from the chemical assault due to alcohol use. Recovery time may depend on how long one has been drinking as well as the individual specific body's ability to restore itself. There are many options for treatment for alcohol use disorders. They depend in part on the severity of the patient's drinking, but treatment options include behavioural therapy and medications (Szigethy E, Frieman E., 2009; Rounsville B, Carroll K, Back S., 2005). The goal of long-term treatment for alcohol dependence is total abstinence. Evidence strongly suggests that seeking total abstinence and avoiding high-risk situations are the optimal goals for people with alcoholism. A strong social network and family support is also important. Families and friends need to be educated on

how to assist, and not enable, the drinker. Support groups can be very helpful in providing advice and guidance.

7.1 Alcohol Withdrawal

Changes in bodily function that is experienced by a patient and is associated with when a person who often drinks too much alcohol suddenly gives up the habit is called withdrawal symptoms. Withdrawal symptoms begin within 6 - 48 hours and peak about 24 - 35 hours after the last drink. At this time, the inhibition of brain activity caused by alcohol is abruptly reversed, stress hormones are oversecreted, and the central nervous system becomes overexcited (Sullivan JT, Sykora K, Schneiderman J., Naranjo C.A., Sellers, E.M., 1989). The NMDA system is also important in alcohol withdrawal (Petrakis IL, Limoncelli D, Gueorguieva R, Jatlow P, Boutros NN, Trevisan L, et al., 2004). Every alcoholic go through withdrawal syndromes on quitting and these can range from unpleasant to life-threatening events (Miller W.R., Tonigan J.S., Longabaugh R., 1995). Application of a harm reduction approach allows people to decrease step by step the number of drinks they consume each day, without requiring the withdrawal syndrome. But the will to cease imbibing in alcoholic drinks may often be there but difficult to attain without assistance. Thus, treatment options become the mainstay for this menace.

7.2 Alcohol Abuse Withdrawal Symptoms Treatment

Treatment for alcohol abuse aims to calm the patient as quickly as possible while being observed for at least 2 hours to determine the severity of withdrawal symptoms. Often people have mild-to-moderate withdrawal symptoms like agitation, trembling, disturbed sleep, and lack of appetite, brief seizures and hallucinations. Some have been shown to progress to full-blown delirium

tremens (Schuckit M.A., 1995).). Anti-anxiety drugs (benzodiazepines) inhibit nerve-cell excitability in the brain and are considered to be the treatment of choice because they relieve withdrawal symptoms and reduce the risk for seizures. Long-acting benzodiazepines (chlordiazepoxide, oxazepam, and halazepam) are preferred because they pose less risk for abuse than the shorter-acting drugs, which include diazepam, alprazolam and lorazepam (Schuckit M.A., 1995; Miller N.S., 1995). Antiseizure drugs, such as carbamazepine or divalproex sodium are often recommended for reducing the requirements of a benzodiazepine (Miller N.S., 1995). "These do not appear to reduce seizures or delirium associated with withdrawal when used by themselves. Beta blockers, such as propranolol and atenolol, are sometimes used in combination with benzodiazepines. They slow heart rate, reduce tremors and may also reduce cravings" (Miller N.S., 1995).

7.3 Specific Treatment for Severe Symptoms

Seizures are usually self-limited and treated with a benzodiazepine (Sachdeva A, Choudhary M, Chandra M., 2015). Benzodiazepines are used primarily in the treatment of the hyper excitability, including convulsions and hallucinations, during withdrawal (Sachdeva A, Choudhary M, Chandra M., 2015). Co administration of intravenous phenytoin with a benzodiazepine may be used in patients who have a history of seizures, who have epilepsy, or in those with ongoing seizures but the patient's heart should be monitored during treatment because of the hypotensive effect of phenytoin. For hallucinations or extremely aggressive behavior, antipsychotic drugs, particularly haloperidol, may be administered (Williams S.H., 2005). "Rapid and immediate injection of the B vitamin thiamine is necessary to treat Wernicke-Korsakoff syndrome caused by severe vitamin B1 (thiamine) deficiencies, which cannot be replaced orally" (Pettinati H.M., Rabinowitz A.R., 2006).

7.4 Anti-craving Medications

The main anti-craving drug is naltrexone which is an opioid antagonist originally developed for treatment of opioid addictions (Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M., 2010). It has been shown to be useful in decreasing craving for alcohol, which is associated by its ability to block opioid function. This drug reduces the intoxicating effects of alcohol and the urge to drink (Bouza C., Angeles M., Magro A., Muñoz A., Amate J.M., 2004). "Naltrexone is approved for the treatment of alcoholism and helps reduce alcohol dependence in the short term for people with moderate-to-severe alcohol dependency. There is an oral form which is taken daily and a once-a-month injectable form of naltrexone. Side effects include nausea, vomiting, stomach pain, headache and fatigue. High doses can cause liver damage" (Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M., 2010; Bouza C., Angeles M., Magro A., Muñoz A., Amate J.M., 2004). Acamprosate is another drug approved for treatment of alcoholism. Acamprosate is a drug that acts by stimulating the GABA inhibitory system and antagonizing the glutamate excitatory system, thus calming the brain and reducing craving for drinks (Lingford-Hughes A.R., Welch S., Peters L., Nutt D.J., 2012). "This drug reduces the frequency of drinking and, in combination with psychotherapy, improves quality of life even in patients with severe alcohol dependence. It may cause occasional diarrhea and headache and can also impair certain memory functions which does not alter short-term working memory or mood. People with kidney problems should use acamprosate cautiously" (Lingford-Hughes A.R., Welch S., Peters L., Nutt D.J. (2012).

7.5 Aversion Medications

“Disulfiram is an inhibitor of aldehyde dehydrogenase, and when taken with alcohol results in the build-up of acetaldehyde levels leading to nausea, dizziness, headache and flushing; making the entire drinking experience very aversive, and thus decreasing the desire to drink. This can happen within an hour or two of drinking half a glass of wine or half a shot of liquor and may last from half an hour to 2 hours, depending on dosage of the drug and the amount of alcohol consumed. Effectiveness of a dose of disulfiram is usually 1 - 2 weeks and overdose can be dangerous, causing low blood pressure, chest pain, shortness of breath, and even death” (Schuckit M.A., 1995; Miller N.S.,1995; Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M., 2010).

7.6 Other Drugs used for alcohol recovery

“Topiramate is an anti-seizure drug used to treat epilepsy. Topiramate is thought to have an effect on alcohol cravings and alcohol use by interacting with GABA” (Miranda R Jr., MacKillop J, Monti PM, Rohsenow DJ, Tidey J, Gwaltney C, et al. (2008). It also potentially decreases the release of dopamine, which is involved in the pleasure caused by alcohol consumption. Studies indicate it may help treat alcohol dependence (Paparrigopoulos T, Tzavellas E, Karaiskos D, Kourlaba G, Liappas I. 2011). In one study, patients who took Topiramate had fewer heavy drinking days, fewer drinks per day, and more continuous days of abstinence than patients who received placebo (Wetherill, R.R., Spilka, N., Jagannathan, K. et al., 2021). “Side effects include burning and itching skin sensations, change in taste sensation, loss of appetite and difficulty concentrating. Baclofen is a muscle relaxant and antispasmodic drug” (Leggio L, Garbutt JC, Addolorato G., 2010). “Among pharmacological agents that have been used in experimental studies for reduction in craving, baclofen appears to have a significant

advantage over other agents" (Addolorato G, Leggio L, Abenavoli L, Agabio R, Caputo F, Capristo E, et al., 2006; Rozatkar AR, Kapoor A, Sidana A, Chavan B.S., 2016). It reduces craving and alcohol consumption and causes few side effects.

8.0 CONCLUSION

Alcohol can limit life and career but in reasonable amounts was accepted as beneficial. People who never took alcohol and had engaged in other healthy life habits seem to fare better than those that had imbibed for some time and quit. This often depends on the length of time spent as drinkers. Genetic variation in alcohol metabolizing enzymes is a main source of inter-individual variability in alcohol metabolism. Gender variation in alcohol handling makes women more susceptible to the effect of alcohol consumption than men. People who are able to moderate their alcohol intake are also more likely to have been able to choose other healthier life style. Drinking alcohol is addictive and even when alcohol use may seem beneficial in moderation the brunt of disease lies with the alcoholic.

COMPETING INTERESTS

This work was carried out in collaboration among all authors. Authors have declared that no competing interests exist.

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