A REVIEW OF ALCOHOLIC BITTERS PROLIFERATION IN NIGERIA: A FRIENDLY MULTIFACETED KILLER LOOMING ACROSS THE NATION

O IBRAHEEM^{1*}, RO ADIGUN¹

ABSTRACT

Proliferation of alcoholic bitters and its increasing consumption is viewed to be a major public health concern in Nigeria. Many of these drinks are illicitly distilled in obscure locations and some manufacturers claim the bitter ingredient is a secret recipe. Due to consumers' belief about its therapeutic effects, there is tendency towards excessive consumption and resultant increase in health risk. In some cases, it leads to unprotected sex among youths thereby increasing unwanted pregnancies and sexually transmitted diseases. The continuous and unguided consumption of this friendly and subtle killer thus contributes to increase in the mortality and morbidity rate, homelessness and joblessness among many in Nigeria, and therefore cognate efforts by government and communities must be put in place to ensure reduction of this menace. Furthermore, ease of access to these alcoholic bitters is what Nigeria policies and lawmakers should take as a priority and urgently address before it ruins the entire well being of the populace and economy at large.

Keywords: Alcohol-abuse, Chronic illness, Death, Illicit drug, Phytochemicals, Therapeutics

INTRODUCTION

Since the beginning of history, humans have searched for substances that will act on their nervous system thereby increasing their natural abilities and confidence in order to tackle disturbing issues and also to produce pleasurable effects.¹ Ajayi and Ekundayo,² described drug as a substance that can reduce pain, anxiety, tension, ignorance, misinformation among others. Among the drugs, alcohol is known to be widely consumed by humans due to its lack of regulation or restrictions in many countries unlike other drugs such as cannabis, marijuana, cocaine, etc. World Health Organization³ ranked Nigeria and two other countries in the sub-Saharan African among the thirty nations with highest per capita consumption level of alcohol worldwide. Also Gureje et al.⁴ and a Nigerian-based marketing research company; MRIC in 2015, reported an increase in alcohol use among Nigerians. The report further stated that most alcohol consumers are now switching to herbal mixed alcoholic drinks.

O IBRAHEEM^{1*}, RO ADIGUN¹

¹Department of Biochemistry, Federal University Oye-Ekiti, PMB 373, Oye-Ekiti, Ekiti State, Nigeria. ***Correspondence to:** Dr. Omodele Ibraheem; Plants for Biotechnological Resources Research Group, Department of Biochemistry, Federal University Oye-Ekiti, Km 3 Are-Afao Road, P.M.B 373 Oye Ekiti, Ekiti state, Nigeria. Telephone: +234 81 3942 7707, Email: <u>deleibraheem2007@yahoo.com</u> In Nigeria, alcohol is often traditionally used to portray a relationship and communion between the living human and ancestors, deities and or other supernatural entities.⁶ In recent times, the Nigerian market has being flooded by different brands of alcoholic bitters and they enjoy high patronage among consumers.⁷ However, few research information or knowledge exists on the effects of these bitters on the body. They arrived surreptitiously into the Nigerian markets and have taken over as drinks of choice to many; even big brewery companies are not left out in mass production of these bitters. This trend saw a rise in the alcoholic brands such as Alomo Bitters, Kerewa, Ibile, Opa Evin, Erujeje Bitters, Man Power Agbo, Arouser, Galant bitters, Action bitters, Washing and Setting, Baby-Oku, Skelewu, Agbara, Do well bitter, Goko Cleanser Ruzu, Star herbal, Orijin as well as Swedish, Chinese and India bitters, among many others. Such bitters are sold in all manners of places which include markets, departmental stores, supermarkets, highways, roadsides, buses, etc. In south-western Nigeria to be precise, one of the most easily accessible forms of medicinal herbs fermented with

alcohol is called "Paraga" with the synonyms "Opa-Ehin, Foganna and Fidigbogi". Paraga is an herbal mixture with assorted ingredients and indeterminate alcohol content. It is popular in many neighborhoods in Nigeria. It is popularly used as a stimulant and is believed to have curative effects on an extraordinary range of ailments.⁸

A small bottle of baby-Oku bitter can be gotten for as low as 100 naira compared to beer which is sold for over 250 naira in the market, depending on the brand. This small bottle of bitter will intoxicate and make the consumers drunk faster than five bottles of beer. This is viewed as money saver, thus many unemployed Nigerians possibly get their brand of alcoholic bitters with little money from the nearest shop in a bid to reduce tension and stress of unemployment, while high school students can possibly get theirs using pocket money. According to Nzegwu et al.⁹ the general view of commercial bus drivers is that a wise driver who wants to make profit must take these bitters, so as to ensure there is energy to drive for long hours in a day. Others say the bitters are blood cleanser, thus many have changed from drinking beers such as Stout to drinking alcoholic bitters; thus each consumer has own different reason(s).

According to Ebirim et al.¹⁰ psychoactive substance misuse in Nigeria especially alcohol has for many years being an issue of increasing health and social importance. Globally, alcohol is responsible for 1.8 million (3.2 %) deaths annually or 4.0 % of the global disease burden and about 50 % of these deaths are due to injuries.¹¹ While alcohol related fatalities are decreasing in high income countries (HIC),¹² there has been alarming increase in alcohol related problems in low-middle income countries (LMIC) to which Nigeria belongs.¹³ This review thus showcases how high alcoholic bitters consumption has affected many lives and homes in Nigeria, and suggests measures that could reduce this menace.

REGIONS WHERE ALCOHOLIC BITTERS ARE HIGHLY

PROLIFERATED AND CONSUMED

Production and consumption of these alcoholic beverages in Nigeria is on the increase,¹⁴ and the volume is highly unrecorded due to illegal and local productions,¹⁵ and also due to the scarcity of data on the legal production. Ebirim et al.¹⁰ found that alcoholic beverages are sold most commonly where the industries are situated. In other words, proximity to alcoholic breweries encourages alcoholism in Nigeria. For instance, the South Western and South Eastern regions of Nigeria (see Figure 1) are industrial hubs and so many big factories including big brewery and alcoholic companies are sited, thus making people residing within these regions have easy access to these alcoholic drinks. The Northern region in contrast, has fewer drinkers, primarily due to their religious belief, which discourages alcohol intake.¹¹



Figure 1: Nigeria Map indicating regions where consumption of Alcoholic bitters is rampant. The alcohol is majorly consumed in the southern region due to the industrialization of the areas and lack of strict cultural and religious beliefs that forbid alcohol consumption

Njoku,¹⁶ paid visit to some of these alcoholic industries; and found that they have very well planned market strategies that are being put in place to ensure effective marketing and distribution. It was discovered that false addresses were written on labels of products from some of the acclaimed factories and on interviewing the staff they gave little or no response to the questions. This means some alcoholic bitters are still illicitly produced in obscure locations. Nzegwu et al.9 reported that alcoholic bitters are sold without any restriction in public bus stations in Edo, Lagos and Ogun states and other southern Nigeria regions. A study conducted by Nzegwu et al.⁹ in Benin, Edo State, reported that the percentage alcohol involvement in road traffic accident morbidity and mortality rate was 23.32 %. Ebirim et al.¹⁰ also conducted a survey on prevalence of alcohol use among students in Owerri, a southeastern part of Nigeria and concluded that 78.4 % of the 482 subjects confirmed that they are current users, with twenty-seven percent of them being heavy drinkers (i.e drink more than 4 bottles per day). Previous study by Ebirim et al.¹⁰ discovered that drinking is much among the Igbos' and Yorubas' ethnic groups of southern Nigeria, which often neglect the safety and quality assurance of the products they consume.

ARE THERE SALES, ADVERTISING LAWS OR REGULATIONS GUIDING ALCOHOLIC BITTERS IN NIGERIA?

According to Ufuoma¹⁷ concerning advertising laws on alcoholic bitters; advertising in Nigeria is regulated by a combination of federal, state laws, subsidiary legislation and guidelines. Thus, before an alcoholic beverage can be advertised to the public through radio, television, and newspapers, it must meet the rules and standard laid down by these agencies. They are Advertising Practitioner's Council of Nigeria (APCON), the National Agency for Food and Drug Administration (NAFDAC) act 1993 and National Broadcasting Commission (NBC).

Alcohol advertisement is a very sensitive issue and it should be designed to promote



socially responsible behavior and protect the young people. There are guidelines concerning the time of the day when alcohol should be advertised. Also, selling or advertisement of alcohol in children's programmes on television, around schools, place of worship or sport arena are highly prohibited according to the Nigerian law guiding alcoholic beverages.¹⁷

Beers, wines and non-alcoholic bitters are advertised in the media, on highways and sign posts on the streets and possess labels stating "drink responsibly" and product should not be consumed if person is below eighteen years old. They also possess the exact ingredients and address of the producer. This indicates the advertised beers must have been strictly analyzed in the laboratories for safety and quality assurance by NAFDAC and have met the standard laid by the APCON and NBC before they can advertise their products publicly. The complicating issue is whether Nigerians understand and know the source of this warning message "drink responsibly" and how efficient it is. For example, in USA, the warning has a heading that reads: GOVERNMENT WARNING, while that of Arizona (a state in USA) has its own heading as WARNING.¹⁸ This is not so in the case of alcoholic bitters in Nigeria where there is absence of restrictions or regulations. Many alcoholic bitters do not write the exact content of their products and some claim it is a secret recipe to prevent adulteration, whereas the producers themselves are the adulterator of their products. They also sell the fake products at the same price with the original so as to divert the attention of the consumers. Some labels do not have the exact address of their manufacturer and yet they possess NAFDAC number. Unlike the beers and some nonalcoholic bitters like "Yoyo bitters", most of the proliferated alcoholic bitters are not publicly advertised in the media, rather they sell their products at cheap prices on obscure locations across the nation. Labels do not contain advice to consumers on how to consume the product in an understandable form. Also the source of the information is unknown, and age at which a teenager should

start consuming the alcoholic bitters is absent.

Sales, advertisement and use of beers, spirits and wines are stated and strictly regulated by the government agencies around the world.¹⁸ But it is taken with levity in the case of alcoholic bitters that have taken over the choice of drinks of many Nigerians, all in the name of having therapeutic effects. It should be noted that the alcoholic content is not at its pure form and complete ingredients not disclosed. Alcoholic bitters are sold in every motor park, around high schools, on streets and even some pharmacies across the nation sell different brands of alcoholic bitters so as to make profit.

IS ALCOHOL CONSUMPTION GENDER SENSITIVITY?

Alcohol consumption is claimed to be part of adult male characteristic and plays a major role in socio economic, political and religious relationships as well as agent for social cohesion.¹² These functions inter alia, encouraged its usage. In the Nigerian society, reasons for drinking may vary from community to community, but it is mainly for pleasure,¹ for elixir or healing. Some of these reasons still exist till date while new ones have emerged. The new drinking norms that have recently evolved, is drinking competition predominantly among males and fast rising in females. Bar owners, breweries or distillers set out prize especially for the fastest drinker and the winner is judged based on the quantity of drinks he or she could take and hold on without any sign of intoxication. This scenario often produces precarious results, yet nothing serious is being done by the policy makers.

According to Emeka²⁰ study, males recorded the highest consumption rate of alcoholic bitters with the aim of drinking to become confident to initiate sexual relationships, stimulate sexual urges, prolong erection, increase sexual satisfaction and become more aggressive during sexual intercourse. Norms in Nigeria confer on men the right to drink alcoholic beverages while women drink flavored beverages. However, some



women also drink in order to be bold in initiating sexual relationships, for sexual arousal and to increase satisfaction.²¹ Besides, not every brand of alcohol is used for sexual purposes. For example, while men use 'herbal' alcoholic beverages and a mixture of locally-produced gin and marijuana, women use champagne and other flavored alcoholic beverages. It has been shown that the observed difference in alcohol tolerance between men and women is related to their body fat contents.²¹ The fat makes the alcohol accumulate in women body and get them intoxicated quickly. If a woman and a man, who both have the same weight, consume the same amount of alcohol, the woman would achieve higher blood alcohol levels compared to the man; thus alcohol intake is gender sensitive.²¹

HEALTH AND SOCIAL CONSEQUENCES OF ALCOHOLIC BITTERS CONSUMPTION

Alcoholic bitters have been around for a long time and is said to have a lot of health benefits. It is said to stimulate appetite especially in those convalescing or persons with reduced appetite.²² Currently, they are much sought after for their health benefits and are becoming common medicines in many Nigerian homes as many are neglecting the regulated orthodox medications. The bitters among many others are claimed to boost sexual libido, strength and mental alertness. It's a common belief that drinking these bitters is like taking natural herbs from God, thus many Nigerians are indulging and patronizing them even in the absence of any government approval.

Although standard drinking habits are not specified in Nigeria due to a lack of written alcohol control policies,²³ it can be inferred that many engage in heavy drinking due to its claimed therapeutic effects. However, this has severe health consequences, as some of these alcoholic beverages contain high Alcohol by Volume (ABV). For instance, Alomo Bitters contain 42 % ABV; gin contains 20-43 % ABV, while stout contains 7.5 %, as some alcoholic bitters which are illicitly made may contain methanol.

The use of high volume of alcohol and minute amount of stipulated medicinal herbs is becoming rampant. Some manufacturers neglect the herbs and mix only colouring and bitter ingredients with alcohol in order to assume the quality of other registered and renowned alcoholic bitters like Alomo bitters. Major and serious health concerns are raised on fake and indiscriminate packaged herbal bitters that have toxic effects on the spleen, pancreas and heart, and which lead to sudden death.²⁴ NAFDAC discovered that some of the products are laden or rather adulterated with 'poisonous methanol' and could cause neurological problems and death, and heavy metals were detected in some alcoholic bitters.²⁵ On many laboratory test analyzes conducted, these toxic substances were often found in analyzed blood samples of dead drivers that were high drinkers of these bitters.²⁶ Nzegwu et al.⁹ findings on the influence of alcohol on road accident in Benin, Edo State, Nigeria, revealed an increase in mortality rate, as high blood alcohol related accidents constituted 18% of accident cases, while 87% of the car drivers were commercial drivers. Alcohol influence road traffic accidents and the consequential injuries are therefore more common with commercial vehicle drivers than with private counterparts.^{9,27}

According to statistical report from NAFDAC between April and June 2015, 89 persons were confirmed to have died in Nigeria following the consumption of alcohol bitters. Furthermore, Ohimain²², reported a Nigerian methanol poisoning case, where fermented alcoholic beverage was found to contain 16.3 % methanol. In the NAFDAC statistics, the blood methanol concentration of victims was found to range between 1500 - 2000 mg/l. NAFDAC consequently has identified "Galant bitters and killer bitters" and some others in the Nigeria market and sent public alert even as it has placed the products on hold.²⁴

The use of methanol as a cheap alternative to ethanol by illegal manufacturers for production of these drinks at obscure locations is now an illegal criminal enterprise

67

many are adopting. Most times, the problem stems from the poor distillation of homemade alcohol by which the distilled portion contains high methanol content, which is not removed. Symptoms of methanol poisoning may include a decreased level of consciousness, poor coordination, vomiting, abdominal pain, and a specific smell of breath.²⁸ Toxicity and death may occur even after drinking a small amount.28 Other components such as heavy metals (lead, arsenic) among others were discovered beyond the permissible limits in some analyzed herbal products purchased from Nigerian markets.²⁹ Public health hazards from ingestion of herbal medicines are identified and disclosed by in-depth risk assessment studies and are regarded unfit for human consumption. Accumulation of these heavy metals in the body may cause the release of free radicals in body cells leading to various degenerative diseases.²⁹

The problem of alcoholism in Nigeria stems from individuals whose excessive drinking lifestyle has damaged both their lives and affected people around them. Many are faced with diverse health challenges due to the prolong intake of these cheap alcoholic bitters having high concentration of over 45 % ABV. As unemployment ravages the society, many who cannot afford to buy bottles of beer to get drunk turn to buy small bottles of alcoholic bitters which are much cheaper, making them to easily get drunk. For that moment they forget the hardships and/or sufferings being experienced, subsequently they fall back to state of depression afterwards the effect of alcohol is gone; developing wretched life style.³⁰The children of alcoholic parents are often neglected and subjected to various abuses, which lead to adverse emotional development. These children may develop a number of emotional problems, such as fear of people, petty theft, bed wetting, prostitution, armed robbery, obscure sexual orientation, etc.³¹

Furthermore, many youths that indulge in these alcoholic bitters often experience sexual urges. Continuous drinking of these bitters with the thought that they improve their sexual stamina and performance, many are often times engaged in unprotected sex and they impregnate or are being impregnated at very youthful age; having no job at hand.

COMPONENTS OF ALCOHOLIC BITTERS AND THEIR XENOBIOTIC EFFECTS ON HUMAN

Plants secondary metabolites (phytochemicals) that confer various therapeutic effects and many other biological functions are located within the plant cell.^{32,33} Such effects include anti-malaria, antioxidant, anti-inflammation, anti-microbial, anti-cancer, prevention of certain cardiovascular and degenerative diseases such as stroke, hypertension, and enhancement of brain functions. Thus, appropriate extraction protocol must be employed using the right solvent that has ability to lyse the cell and which is also tolerant for human consumption.³⁴ Though many people use dry plant herbs, liquid plants extracts are more popular and effective. However, not all plants phytochemicals are soluble in water; some are insoluble in water but soluble in organic solvents. For this reason alcohol:water mixture is often used. The alcohol which is organic solvent extracts the water insoluble constituents and water extracts the soluble metabolites. The biological and therapeutic activity of any plant is closely related to the phytochemicals it possess, and these phytochemicals are broadly classified into major groups as essential oils, alkaloids, acids, steroids, tannins, saponins, etc.³²

With respect to human body chemistry and consumption of alcoholic bitters, two major xenobiotics are involved, and they are the phytochemicals and alcohol used as the solvent vehicle. Xenobiotics are foreign substances that when ingested by human alter the metabolic and biochemical reactions in the body. Consumers take these bitters without prescribed dosage unlike the orthodox medicines. Though the body could utilize some of the phytochemicals with no cytotoxicity, but some classes of alkaloids like nicotine, caffeine, morphine among



others when ingested could alter the activities of the nervous systems.³⁵ It has been found that low oral bioavailability and poor systemic delivery to target tissues and organs represent the major drawbacks associated with the clinical failure of many promising phytochemicals.³⁶ Thus, there is high possibility of this failure in heavy drinkers due to the increased absorption, solubility, rapid metabolism and distribution of alcohol and its metabolites over the phytochemicals.

Petti and Scully³⁷ showed that spirit drinkers usually consume high amount of alcohol in a unique occasion, with unbalanced high concentrations of ethanol over the phytochemicals. Thus the possibility of toxicity and diseases generated from heavy consumption of alcoholic bitters can be measured from the drinking pattern (dosage) of the consumers.²⁰ According to World Health Organization (WHO),³ the heavy drinking group comprises mainly young subjects with an intake of at least 60 or more grams of pure ethanol (>5 drinks) on, at least, one occasion in the past seven days, generally during the weekend. However, in Nigeria alcohol is consumed almost every evening of the day at public gatherings or among peer groups. In the middle drinking group, a regular and low to moderate consumption can be advocated such that one to two drinks per day, while the light drinking group alcohol intake usually corresponds up to one drink per day.^{38, 39} The drinking pattern strongly affects health outcomes, and much attention would be placed on the light drinking and the heavy binge drinking groups as shown in Figure 2. If the amount of ethanol consumed is light, recycling can keep up with the disposal of ethanol by the liver and plants phytochemicals can perform their biological activities and therapeutic effects. The ethanol disposal rate in a 70 kg human is about 15 ml of ethanol per hour, which corresponds to 360 ml of beer, 120 ml of wine or 30 ml of spirits containing different percentage of alcohol. Alcoholic bitters have over 45 % Alcohol by Volume (ABV) higher than the ones of beers and wines having 5 % and 9 % - 16 % respectively.

For adverse effect to occur after alcohol

intake, the blood alcohol concentration level must rise to 0.18 % to 0.30 % and possibly lead to coma if Blood Alcohol Concentration (BAC) reaches 0.35 % to 0.80 %.⁴⁰ A 5 ml dose of herbal extracts contains about as much alcohol as 1/6 of a glass of beer or wine. Such a small intake of alcohol is rapidly metabolized by the liver and consequently its effect on the blood alcohol level may not be traceable. Regardless of the kind of alcoholic drink intake, a high alcoholic drink would overload the liver's metabolizing capacity by reducing xenobiotics biotransformation enzyme cytochrome P450, which then causes significant blood alcohol levels and subsequent adverse effects like fatty liver diseases, cirrhosis and hepatic carcinoma, and brain damage possibly leading to coma and finally death (Figure 2).^{41,42}

Therefore, the chances of products of alcohol degradation (such as acetaldehyde) forming reactive oxygen species that clash with and displace the necessary phytochemicals required for scavenging free radicals, will eventually lead to all kinds of cancer.³⁸ Thus, drinking alcoholic bitters for medicinal purposes like blood formation, cancer prevention, anti-bacterial, anti-malaria etc, heavy drinkers are disposed to alcohol generated diseases, which could cause damage to their immune system thereby exposing them to numerous infections.

Table 1 shows the summary of the metabolic impairment that could be caused by excessive metabolism of alcohol in the body. In the metabolism of alcohol, NADH is generated, but on large consumption excess NADH will be generated which thus limits the concentration of NAD⁺ that is required for activation of other vital biochemical pathways. As a result, some biochemical processes will be blocked while others will be over activated.



Figure 2: A schematic illustration of possibly metabolic fate of alcoholic bitters in human body

<u>Table 1: Metabolic effect of over production of NADH generated from ethanol metabolismand</u> the clinical consequence

Metabolic Effect	Clinical Consequence
Decrease gluconeogenesis	Hypoglycemia
Increased lactate	Elevated blood lactate, gout
Increased ketoacids, decrease Krebs (TCA) cycle	Ketoacidosis
Inhibition of many oxidative reactions that use \mathbf{NAD}^{+}	Inhibition of some drugs and hormone metabolism
Decreased fatty acid oxidation and increased fatty acid synthesis	Fatty liver, elevated blood lipids

In general, ethanol consumption irrespective of the type of beverage accounts for about 5 % of various cancers, mainly of the liver,⁴¹ upper digestive and gastroenteric tracts, pancreas, breast, and lung, ^{43,44} particularly when consumed above the recommended upper limits.^{45,46} In 2011, Western Europe had 30 % of oral cavity and pharynx cancers attributable to alcohol drinking, ⁴⁷ which increases to about 44 % for the upper aerodigestive tract (i.e. localized at oral cavity, pharynx, larynx, and esophagus) cancers.⁴⁵

WHY DO MANUFACTURERS INCREASE ALCOHOLIC CONTENT IN BITTERS?

Manufacturers are now increasing the alcoholic content of bitters ignoring the health well being or social consequences on their consumers. Many have decided to reduce the concentration of the plants extracts used in order to make more products and maximize profits. Three broad reasons have been put forward, and these include:

Enhances phytochemicals extraction from plant cell lysate

Although other liquids, such as glycerin, vinegar, acetone among others have been tried but alcohol (ethanol or ethyl alcohol) is still considered the best.⁴⁸ However, it is very important to note that not all alcohol grades/types are edible, such as methanol. Though it is part of alcohol group and even much cheaper in price than ethanol, it is often produced with lots of contaminating substances which are difficult for the liver to metabolize. Consequently, the metabolized formic acid product of methanol is highly detrimental to human health.⁴⁹ Methanol when ingested can have adverse effects on the individual causing immediate death.⁴⁹

Alcohol being a bi-polar compound is miscible in water (polar) and oil (non-polar), thus it could easily extract both polar and non polar portions of the plant cell lysate.⁵⁰ These properties lured many manufacturers to use high volume of alcohol for the preparation of bitters and a higher concentration of ethanol (possibly without water) would extract many bitter and astringents compounds from the plant cell lysate. Furthermore, these high ethanol content bitters could react with the phytochemicals and degenerate to methanol while still in the store.

Some illicit distillers use ethanol-methanol mixture or methanol directly to extract the phytochemicals since methanol has almost same properties as ethanol, neglecting the health and safety of the consumers. They package their fake products, distribute them through their various outlets and sell at the same price with the original brands in order to make more profit.

Enhances bioabsorption of phytochemicals

Distillers take advantage of alcohol's properties of high absorption and distribution rate when ingested orally to manufacture their products. These properties possessed by alcohol indirectly enhances plants phytochemicals such as tannin, steroids, saponins, alkaloids, flavonoids, glycosides, essential oils passage through the membranes after hydrolysis in the intestine at a faster rate, moving freely through the blood streams to their site of action. This indirectly enhances the therapeutic effects of the medicinal plants rather than using water for its preparation.

In order to make their products effective and accepted by consumers, they extract with high concentration of ethanol (sometimes > 45 %). Ethanol crosses biological membranes by passive-down concentration gradient diffusion. The higher the concentration of alcohol, the greater is the resulting concentration gradient, and the more rapid is the absorption.⁵⁰ Therefore, more ethanol is found in the blood than in the muscles and adipose tissues and its metabolites cross the brain barrier to alter every metabolic activities leading to coma, eventually death. This event frequently happens to high alcoholic drinkers as they have drunk above the limits and often times the drinks may contain denatured alcohol.⁵⁰

> Enhances shelf life of products

Alcohol in its pure form irrespective of type does not alter its chemical composition,



denatures or expires, but begins to have shelf life when mixed with other ingredients.⁵¹ Vodka, gins possess high percentage of alcohol and are not mixed with any other ingredients and as such may last forever. Thus, the higher the alcoholic content, the higher the shelf life of the product. Though the alcoholic bitters have high alcohol content, once the bottle is opened, air gets in and subsequently the alcoholic content begin to drop. Hence, manufacturers tend to increase the alcoholic content in order to enhance the quality of their products without looking at the possible side effects the alcohol may cause to the health of the consumers. This result in consumers drinking the entire content of the product immediately it is opened in other to get the right quality, and this eventually lead to drinking alcohol above the limit, putting enormous pressure on the liver.

UNPERTURBED ATTITUDE OF CONSUMERS TO RISKS ASSOCIATED WITH ALCOHOLIC BITTERS CONSUMPTION

Many alcohol users are aware of the risk behind taking alcoholic drinks but the fact that bitters are claimed to be medicinal still confuses them from abstaining. Ebirim et al.¹⁰ conducted a study on University undergraduates on the perceived effects of alcohol consumption on their health status. 68.5 % accepted that it forms high risk factor for most health problems like lung cancer, liver, sexually transmitted disease, HIV/AIDS, low birth weight in women, stroke and sudden death. 63.8% admitted it causes drowsiness and weakness, 64.3% accepted it may precipitate defective memory and impaired perception, implying alcohol consumption alters the brain's activities. Over 70 % of the correspondents accepted taking alcoholic bitters mainly to improve libido among others. Even though majority (83.4%) accepted the establishment of awareness programmes in their institution on alcohol abuse with seminars, workshops, crusades and conferences held at their school premises. Yet, they still make it their drink of choice.

Some consumers have experienced fever, followed by heavy sweating, blurred vision and continuously defecation after every three minutes after taken alcoholic bitters.⁵² This was attributed to some product adulteration using majorly denatured alcohol and without adequate quality control.The fact that Nigerians are aware of these illicit production of these alcoholic bitters and its detrimental consequences, it still has not detered them from consuming these products.

SUGGESTED MEASURES THAT COULD REDUCE THE PROLIFERATION OF ALCOHOLIC BITTERS AND ITS CONSEQUENCES

Though efforts are beingmade by government and non-governmental agencies to reduce the abuse of alcohol in Nigeria, but little measures have been taken to reduce the influx of different brands of alcoholic bitters, and this has been a major contribution to the excessive consumption of alcohol in Nigeria. Attention is not given to these alcoholic bitters due to the fact that Nigerians lay claim to it being a very potent medicinal drink forgetting the fact that it was made with alcohol which when highly consumed can alter the activities of the nervous system. The high acceptance and consumption of these products are driving forces that promote counterfeit production by illicit manufacturers who sell at cheaper price, resulting in proliferation across Nigeria regions.

Suggested measures that could reduce this proliferation are:

Regulating its availability

Alcoholic bitters are virtually sold in every corner of the street in Nigeria, most especially the south western and south eastern part of Nigeria. They are sold on streets, in pharmacies, commercial motor parks, in buses and so on. The high availability of these alcoholic bitters will no doubt convince Nigerians to purchase them. Hence, if Government regulatory agencies such like NAFDAC, NDLEA can lay rules and regulations for the sale of these bitters that can reduce their free and easy



drinks large amounts over a long time period having difficulty in cutting down. Alcoholism takes up a great deal of time as usage is always strongly desired and results in irresponsibilities, social and health problems, and many other unforeseen risky situations. Alcoholic bitters dependants have mindsets that the drinks' bitterness (which comes from the natural herbs) and alcoholic content enhance their efficacy in treatment of illness. Many even take them when they have no ailment at all saying it helps stimulate the immune system in creating defense mechanism against any form of illness or disease that may likely occur in the future.

Treatment or management for alcoholism varies, but each method is meant to help drinker stop drinking altogether (abstinence). Alcohol which is the active ingredient in the drinks and of much volume, penetrate easily through the brain barrier and alters various molecular activities of the brain. These includes the inhibitory and excitatory neurotransmitters binding on their receptors and other part of the brain controlling voluntary and involuntary actions, which may reflect in the decisions and actions of the addict and possibly put lives of people around at risk.⁵⁴ Thus, careful treatment and management of an addict must ensure using possible strategies as discussed below:

Close psychological rehabilitation involving psychotherapist and primary care physician

Putting strong policies that will mitigate against these alcoholic bitters may reduce drastically the access to and proliferation of these alcoholic bitters, thereby preventing / reducing cases of addiction in the country. High quality psychological rehabilitation is mostly required for patients who have being addicted to these drinks. Therapists who specialize in addiction recovery in conjunction with primary care physicians can often help people who are addicted set achievable and empowering short-term goals as they work to overcome their addiction. Once sobriety is achieved, the therapists together with the person being treated can work together to set long-term goals that may

include rebuilding damaged relationships, accepting responsibilities for actions and releasing guilt. Various forms of group therapy or psychotherapy can be used to deal with underlying psychological issues that are related to alcohol addiction, as well as provide relapse prevention skills.

Alternative therapy which may include nutritional and herbal remedies

Alternative therapy could often be used in combination with counseling and other support programs that address any underlying psychological causes of addiction. Alcoholic bitters addicts love for something bitter may lure them to accept herbal remedies easily than the orthodox medicines. The reason being that addicts believe that the bitters contains natural ingredients and are more efficient and safe compared to the orthodox drugs that are synthesized with combination of chemicals. This thus makes them consume anything natural and bitter. Therefore, they may accept the herbal remedies alongside psychotherapy and as therapy improves with time, orthodox drugs may be introduced.

Some drugs made with combination of natural herbs have been proposed to be effective in alcohol addiction therapy. Kushner et al.⁵⁵ blended herbal complex named Declinol which contains a number of key ingredients such as Kudzu, Bitter Herbs (Gentian, Tangerine Peel) and Bupleurum (Radix Bupleuri) and other herbals and conducted its anti-alcohol capabilities in 10 heavy drinkers. Result indicated that it significantly reduce Alcohol Use Disorders Identification Test (AUDIT) scores in moderate and heavy drinkers. From the biochemical analysis, credit was given to the Kudzu which contains daidzin that inhibits aldehyde dehydrogenase-2 (ALDH-2) and suppresses the heavy drinking tendencies; a study that was initially conducted and was successful in rodents.⁵⁶ In addition there is significant evidence that the inclusion of bitters such as Gentian and Tangerine Peel in Declinol not only gives it the bitter taste but also stimulates gut Taste-2 receptor (TAS2R)



and mediate transcription linked to the upstream cAMP/PKA/ERK/CREB pathway in hippocampal neurons⁵⁷ together they act as an aversive mechanism against alcohol intake. Finally the addition of Radix Bupleuri in the Declinol formula has being deduced to have some protective benefits not only in terms of ethanol induced liver toxicity but neuro-chemical actions. This involves endorphins, dopamine and epinephrine which may have profound mechanistic meaning for drug seeking behavior.⁵⁸ The effect of this herbal supplement is similar to the effect of orthodox drugs Disulfiram that prevents the elimination of acetaldehyde, a chemical the body produces when breaking down ethanol.58

Alcohol addiction, regardless of the type of alcohol usually results into malnutrition because alcoholic judgment about diet is affected.55 According to Garcia and Fernandez,⁵⁹ majority of the people with alcohol addiction usually have a state of low blood sugar level (hypoglycemia). Thus, nutritional supplementation may be required alongside psychotherapy and herbal therapy by administering foods that contains high unrefined complex carbohydrate, including whole grains intake.⁶⁰ Also, fresh vegetables and fruits containing antioxidants like betacarotene, vitamins C and E, lycopene, zinc and selenium that can scavenge the free radicals and stress generated from the excessive alcohol intake.⁶⁰

Withdrawal symptoms like nausea, shaking, and vomiting may likely occur in patients. This therapy is therefore proposed to be very efficient in the treatment of alcohol addiction and prevention or reduction of withdrawal symptoms in patients. Though it was carried out on a small scale, further studies and confirmation in a much larger cohort may have important treatment ramifications for not only alcoholism but possibly behavioral excesses as well.

> Introduction of Orthodox drugs

Orthodox drugs can be introduced during or after psychotherapy. However willingness of the patient to adopt orthodox treatment may be low as they tend to have negative mindset towards orthodox drugs. This is one of the reasons of getting addicted to alcoholic bitters ahead of orthodox medicines in treatment of illness or libido enhancer among teenagers. Thus administration of orthodox medicine must be done with utmost patience and care. There are four currently approved medications for alcoholism: disulfiram, two forms of naltrexone, and acamprosate. Several other drugs are also used and many are under investigation.

- **Disulfiram (Antabuse):** it prevents the elimination of acetaldehyde, a chemical the body produces when breaking down ethanol. Acetaldehyde itself is the cause of many hangover symptoms from alcohol use. The overall effect is severe discomfort when alcohol is ingested: an extremely fast-acting and long-lasting uncomfortable hangover.⁶¹ This discourages an alcohol addict from drinking excessively while taking the drug.
- Naltrexone (ReVia and Vivitrol): it is a competitive antagonist for opioid receptors, effectively blocking the effects of endorphins and opiates. Naltrexone is used to decrease cravings for alcohol and encourage abstinence. Alcohol causes the body to release endorphins, which in turn release dopamine and activate the reward pathways. Hence when naltrexone is in the body there is a reduction in the pleasurable effects from consuming alcohol.⁶²Reports have shown reduced risk of relapse among alcohol dependent persons and a decrease in excessive drinking.⁶³Nalmefene also appears effective and works by a similar manner.63
- Acamprosate (Campral): it stabilizes the brain chemistry that is altered due to alcohol dependence via



accessibilities, it will be a great step in combating this menace. Furthermore, illicit selling of the drinks should be countered by launching mobile task force units NDLEA or NAFDAC that will move from street to street in Nigeria, enforcing the law and punishing defaulters without delay. Wholesalers and retailers should be compelled to register and meet the appropriate law requirements with the government agencies before selling the products, and if any unlicensed seller is apprehended, the trader should be heavily fined and the commodities seized. These measures hopefully may reduce the proliferation of these alcoholic bitters.

> Pricing and Taxation

Alcoholic bitters are in no doubt cheaper than beers and wines and it is very possible for an unemployed youth to get two bottles of "Kerewa" sold for 100 Naira each and get more intoxicated than buying 5 bottles of beers which go for 1250 Naira at 250 Naira each that may not give him same pleasure as "Kerewa", even as the alcoholic content of Kerewa is higher; it could also be contaminated.

Taxation is the mechanism most often used by governments in developed countries to deal with alcohol-related social, economic, and health issues, because it has proven to be an effective method for raising revenue and curbing harmful consumption. Most countries' governments increase retail prices of alcoholic beverages over their production and distribution costs and control profit through special alcohol taxes or other price controls.⁵³ Thus higher excise duty and value added tax (VAT) should be levied on these products. An increase in taxes directly increases the prices of the product which may drive down the demand and purchase.

Creating awareness and effective warning signs

Government should improve on the warning signs on alcoholic beverages. Nigeria government use the words "drink responsibly" without stating the source of the information. Unlike the other countries, like the United State of America, that state "GOVERNMENT WARNINGS:" on every alcoholic drinks. Consumers' drink them thinking it was the manufacturers that wrote the signs on the drinks. Besides, an alcoholic bitter carries no warning signs on them. So, consumers are at liberty to drink without fear of violating the law.

Government agencies should also improve on raising public awareness of problems associated with the consumption of these alcoholic bitters aside from them just knowing the health benefits. They should be aware of the various diseases that could result from the excessive consumption of alcoholic bitters. Since the manufacturers claim alcoholic bitters are medicinal, regulations involving dose, dosage, side effects and over dose should be placed on each of the drinks, with the hope that alcoholic bitters in Nigeria will be less abused.

> Quality assurance check

In the case of orthodox medicines in Nigeria, specific digits are placed on each drug sold which will be sent to the NAFDAC to check its validity and quality assurance. NAFDAC has been doing great in that aspect and this has reduced the proliferation of fake medicines. It will be of great service to Nigerians if same principle is adopted for alcoholic bitters, since they are now the alternative choice of many Nigerians to orthodox medicines. Before the registration digits are placed on these drinks, government agencies must have done adequate quality control on each of the brands to ascertain its efficacy. This if carried out judiciously will reduce their proliferation around the country and reduce the nefarious and illicit production.

TREATMENT / MANAGEMENT OF ALCOHOLIC BITTERS ADDICTS

A situation where an alcoholic cannot do without taking alcohol is called Alcohol dependence or Addiction, which on prolong use may result into a condition known as Alcoholism, which is a broad term for any drinking of alcohol that results in problems.⁵⁴ Jill⁵⁴ also ascribed alcoholism to a person that



antagonizing the actions of glutamate, a neurotransmitter which is hyperactive in the post-withdrawal phase.⁶⁴By reducing excessive N-Methyl-D-aspartate (NMDA) activity which occurs at the onset of alcohol withdrawal, acamprosate can reduce or prevent alcohol withdrawal related neurotoxicity.⁶⁵Acamprosate reduces the risk of relapse amongst alcohol dependent persons.^{63,66}

CONCLUSION

Proliferation of alcoholic bitters and its increasing consumption is viewed to be a major public health concern in Nigeria. The continuous and unguided consumption of this friendly and subtle killer contributes to increases in the mortality and morbidity rate, homelessness and joblessness among many in Nigeria and therefore cognate efforts by government and communities must be put in place to ensure reduction of this menace. We urged the government agencies to formulate very strict policies and laws that will regulate sales and purchases of these "friendly but subtle killer" alcoholic bitters. Government should develop and put in place national monitoring systems that will be used to keep track records of alcohol consumption and its detrimental consequences in each region of Nigeria. This will be used to raise awareness amongst the general public, that though these alcoholic bitters may have some acclaimed therapeutic effects, but their "excessive usage is as writing an open letter to chronic illness and sudden death".

ACKNOWLEDGEMENTS

Authors sincerely thank Federal University Oye Ekiti, Nigeria for academic support. Drug Free Club (DFC), Ilesa, Osun State, Nigeria is appreciated for its efforts in sensitizing the Ilesa community and environs in dangers associated to alcohols and drugs excessive usage. R.O. Adigun was the Chief Speaker of DFC 2017.

REFERENCES

1. Odejide AO, Odejide B. Harnessing Pleasure for Population Health Ends. In Peele, S. and Grant, M. (Eds.) Alcohol and Pleasure: A Health Perspective. Philadelphia: Brunner/Mazel.1999.341-355.

- 2. Ajayi IA, Ekundayo HT. Cotemporary issues in Educational management, Lagos. Nigeria. Bolbay publisher; 2010. p. 130
- World Health Organization, Global Status Report on Alcohol 2004. Geneva: World Health Organization. 2004.
- 4. Gureje O, Degenhardt L, Olley B, Uwakwe R, et al. A descriptive epidemiology of substance use and use disorders in Nigeria during the early 21st century. Drug Alcohol Dependence. 2007; 91: 1-9.
- Shakirudeen T. Beer Consumption: Nigeriais the highest alcoholdrinking country in Africa. Pulse.ng (o n l i n e) 2 0 1 7 . pulse.ng/bi/lifestyle/beerconsumption-nigeria-is-the-highestalcohol-drinking-country-in-africaid6667060.html
- 6. Obot IS. Alcohol use and related problems in sub-Saharan Africa. Afr. J. Drug Alcohol Stud. 2006; 5:17-26.
- 7. Ogazi C, Edison E. The drink driving situation in Nigeria. Traffic Injury Prevent. 2012; 13:115-9.
- Oshodi OY. FAO: "Paraga" ('Masked Alcohol') Use and The Associated Socio-cultural Factors Among The Yoruba Of South West Nigeria: A Case Study of Secondary School Students in Lagos. Q. J. of Fundam of Mental Health .2007; 1:1.
- Nzegwu MA, Akhiwu W, Nzegwu CO, Banjo AA, Aligbe JU. Influence of Alcohol on Road Traffic Accident Morbidity and Mortality in Benin-City Nigeria. A One-Year Study between August 2003 - July 2004. Adv. In Biores. 2011; 2:73–78.
- 10. Ebirim IC, Morakinyo OM. Prevalence and perceived health effect of alcohol use among male undergraduate students in Owerri, South-East Nigeria: a descriptive cross-sectional study. BMC Public Health.2011; 11:118.
- Gmel G, Rehm J. Harmful alcohol use. Alcohol Res. Health 2003; 27:52-62.



- 12. Kerr WC, Greenfield TK, Midanik LT. How many drinks does it take you to feel drunk? Trends and predictors for subjective drunkenness. Addiction2006; 101:1428-1437.
- 13. Smith R. Alcohol in the Third World: a chance to avoid a miserable trap. Bri. Med. J.1982; 284: 183-185.
- 14. Chikere EIC, Mayowa O. Prevalence and Perceived health effect of Alcohol use among male undergraduate students in Owerri, south-East, Nigeria: a descriptive cross-sectional study. BMC Public Health.2011; 11:118.
- 15. Jernigan DH, Obot IS. Thirsting for the African Market. Afr. J. Drug Alcohol Stud. 2006; 5:57-70.
- 16. Njoku E. A Study of Proverbs 23:29-35 And The Effects Of Alcoholism In Nigerian Society: The Role of the C h u r c h .
 2012.http://www.unn.edu.ng/publica tions/files/images/Njoku%20Emma nuel.pdf. Accessed 31st May 2017.
- 17. Ufuoma A. Nigeria's Advertising laws, regulations and guidelines: the simple "Don't's", (online) Nigerian Law Intellectual Property Watch Inc.2013.
- Fenaughty AM, MacKinnon DP. Immediate Effects of the Arizona Alcohol Warning Poster. J. Public Policy Marketing. 1993; 12:69-77.
- 19. Oshodin OG. Nigeria. In Heath, D.B. (Ed.) International Handbook on Alcohol and Culture. Westport CT: Greenwood Press. 1995.
- 20. Emeka D. Changing Patterns of Alcohol Consumption in Nigeria: An Exploration of Responsible factors and Consequences. Br. Sociol. Assoc. Med. Soc. Group.2013; 7:20-33.
- 21. Dumbili EW. What a man can do, a woman can do better: gendered alcohol consumption and (de) construction of social identity among young Nigerians. BMCPublic Health. 2015; 15:167.
- Health. 2015; 15:167.
 22. Ohimain EI. Methanol contamination in indigenous fermented alcoholic beverages. Food Safety and Regulatory Measures International conference, Birmingham United kingdom. 2015.

- 23. Dumbili EW. Can brewer-sponsored "drink responsibly" warning message be effective without alcohol policies in Nigeria? Drugs Educ. Prev. Policy. 2014; 21:434–439.
- 24. Chukwuma M. NAFDAC probes Galant bitters. 2015. The Guardian n e w s p a p e r http://theguardianonlineng.net/nafda c.probes.galant.bitters/. Accessed 7 Jun 2017.
- 25. Chukwujindu MAI, Anwuli LO, Francisca IB. A survey of metal profiles in some traditional alcoholic beverages in Nigeria. Food Sci. Nutri. 2014; 2:724-733
- 26. Ololade O, Akinrinade K. Nigeria's Herbal gin nightmare. The Nation N e w s p a p e r . 2 0 1 4 . <u>http://thenationonlineng.net/nigeriasherbal-ginnightmare/</u>. Accessed 12 Apr 2014.
- 27. Bekkybabe 28 Years Old Nigerian Dies during Alcohol Drinking C o n t e s t . 2 0 1 2 . http://www.bekkyblog.com/2012/02 /28/28-nigerian-dies.alcoh... Accessed 28 May 2017.
- 28/28-nigerian-dies.alcoh... Accessed 28 May 2017.
 28. Kruse JA. "Methanol and ethylene glycol intoxication." Crit. Care Clin. 2012; 28:661-711.
- 29. Obi É, Akujnyili D, DN, Ekpo B, Orish EO. Heavy metal hazards of Nigerian herbal medicines. Sci. of the Total Env.2006; 369:35-41.
- Total Env.2006; 369:35-41. 30. Audu R. "Alcoholism: A habit too expensive and too damaging." 2011. P.M News Accessed 26 Oct 2011
- 31. Young R, Sweeting H, West P. A longitudinal study of alcohol use and antisocial behavior in young people. Alcohol Alcohol. 2008; 43:204-214.
- 32. Grassi D, Desideri G, Croce G, Tiberti S, et al. Flavonoids, vascular function and cardiovascular protection. Curr. Pharm. Des. 2009; 15:1072-1084.
- 33. Marongiu B, Porcedda S, Piras A, Rosa A, et al. Antioxidant activity of supercritical extract of *Melissa* officinalis subsp. officinalis and *Melissaofficinalis* subsp. *inodora*. Phytotherapy Res. 2004; 18:789–792.
- 34. Elena MV, Giovanni L, Marcello I. Ethanol versus Phytochemicals in Wine: Oral Cancer Risk in a Light Drinking Perspective.Int. J. Mol. Sci.2015; 16: 17029-17047.



- 35. Zenk MH, JuengerM. Evolution and current status of the phytochemistry of nitrogenous compounds. Phytochemistry. 2007; 68:2757-2772.
- 36. Meng XF, Maliakal P, Lu H, Lee MJ, Yang CS. Urinary and plasma levels of resveratrol and quercetin in humans, mice, and rats after ingestion of pure compounds and grape juice. J. A gric. Food Chem. 2004; 52:935–942.
- 37. Petti S, Scully C. Oral cancer: The association between nation-based alcohol-drinking profiles and oral cancer mortality. Oral Oncol. 2005; 41:828–834.
- 38. Bagnardi V, Rota M, Botteri E, Tramacere I, et al. Light alcohol drinking and cancer: A meta-analysis. Annals of Oncol. 2013;24:301–308.
- 39. Turati F, Garavello W, Tramacere I, Pelucchi C, et al.A meta-analysis of alcohol drinking and oral and pharyngeal cancers: Results from subgroup analyses. Alcohol Alcohol. 2013; 48:107–118.
- 40. Djousse L, Gaziano JM. Alcohol consumption and heart failure. Curr.Atherosclerosis Rep. 2008; 10:117–20.
- 41. Vonghia L, Michielsen P, Dom G, Francque S. Diagnostic challenges in alcohol use disorder and alcoholic liver disease. World J. of Gastroenterology. 2014; 20:8024-8032.
- 42. Whelan G. Alcohol: A much neglected risk factor in elderly mental d i s o r d e r s . C u r r O p i n Psychiatry.2003; 16:609–614.
- 43. Anantharaman D, Marron M, Lagiou P, Samoli E, Ahrens W, Pohlabeln H, et al. Population attributable risk of tobacco and alcohol for upper aerodigestive tract cancer. Oral Oncol. 2011; 47:725–731.
- 44. Boffetta P, Hashibe M, La Vecchia C, Zatonski W, Rehm J. The burden of cancer attributable to alcohol drinking. Int. J. Cancer. 2006; 119:884–887.
- 45. Schutze M, Boeing H, Pischon T,

Rehm J, et al. Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. Bri. M e d . J . 2 0 1 1 ; 3 4 2 , doi:10.1136/bmj.d1584.

- Giacosa A, Adam-Blondon AF, Baer-Sinnott S, Barale R, et al. Alcohol and wine in relation to cancer and other diseases. Eur. J. Cancer Prev. 2012; 21:103–108.
- 47. Parkin DM. Cancers attributable to consumption of alcohol in the UK in 2010. Bri. J. Cancer2011; 10:S14–S18.
- 48. Kenneth T. Diversity of Metabolism in Procaryotes. Todar's Online Textbook of Bacteriology. "The Good, the Bad, and the Deadly. 2012. Accessed 15 Mar 2017
- 49. Feany M B, Anthony DC, Frosch MP, Zane W, De Girolami U. Two cases with necrosis and hemorrhage in the putamen and white matter. Brain Pathol. 2001; 11:121–125.
- 50. Martin L. Wonders of extraction: Ethanol.2008. *Khymos (online)*. Blog.khymos.org/2008/06/08/wonde rs-of-extraction-ethanol/ Accessed 31st March 2017
- Annie MH. Does alcohol go bad? 2017. www.thoughtco.com/doesalcohol-go-bad-607437 Accessed 5 Mar 2017.
- 52. Nairaland. Please beware of that bottle of alomo bitters you are about drinking. Health. 2012. www.nairaland.com/1115759/please - b e w ar e - b ottle - alomobittersAccessed 31st May 2017.
- 53. Babor T, Caetano R, Casswell S, Edwards G, et al. 'Alcohol: No Ordinary Commodity Research and Public Policy'. Oxford University Press;2010. p101.
- 54. Jill L. Understanding and Treating Alcoholism: An Empirically Based Clinician's Handbook for the Treatment of Alcoholism: Biological, Psychological, and Social Aspects of Alcohol Consumption and

78

Abuse.Hoboken: Taylor and Francis. 2014;1:55.

- 55. Kushner S, Han D, Oscar-Berman M, William DB, Margaret AM, Giordano J, Beley T, Jones S, Barh D, Simpatico T, Dushaj K, Lohmann R, Braverman ER, Schoenthaler S, Ellison D, Blum K. Declinol, a Complex Containing Kudzu, Bitter Herbs (Gentian, Tangerine Peel) and Bupleurum, Significantly Reduced Alcohol Use Disorders Identification Test (AUDIT) Scores in Moderate to Heavy Drinkers: A Pilot Study. J. Addiction Res. Therapy. 2013; 4:doi:10.4172/2155-6105.1000153.
- 56. Keung WM, Vallee BL. Kudzu root: an ancient Chinese source of modern anti-dipsotropic agents. Phytochemistry. 1998; 47:499–506.
- 57. Kawahata I, Yoshida M, Sun W, Nakajima A, Lai Y, Osaka N, Matsuzaki K, Yokosuka A, Mimaki Y, Naganuma A, Tomoioka Y, Yamakuni T. Potent activity of nobiletin-rich Citrus reticulata peel extract to facilitate cAMP/PKA/ERK/CREB signaling associated with learning and memory in cultured hippocampal neurons: identification of the substances responsible for the pharmacological action.J. Neural Transmission. 2013; 120: 1397-1409.
- 58. Blum K, Noble EP, Sheridan PJ, Montgomery A, Ritchie T, Jagadeeswaran P, Nogami H, Briggs AH, Cohn JB. Allelic association of human dopamine D2 receptor gene in alcoholism. J. Am. Med. Assoc.1990;263:2055-2060.
- 59. Garcia-Ruiz C, Fernandez-Checa JC. To binge or not to binge: Binge drinking disrupts glucose homeostasis by impairing hypothalamic but not liver insulin signaling. Hepatology. 2013; 57:2535-2538.
- 60. Downs BW, Chen AL, Chen TJ, Waite RL, Braverman ER, Kerner M, Braverman D, Rhoades P, Prihoda TJ,

Paloma T, Oscar-Berman M, Reinking J, Blum SH, Dinubile NA, Liu HH, Blum K. Nutrigenomic targeting of carbohydrate craving behavior: can we manage obesity and aberrant craving behaviors with n e u r o c h e m i c a 1 p a t h w a y manipulation by Immunological Compatible Substances (nutrients) using a Genetic Positioning System (GPS) Map? Med. Hypotheses. 2009; 73:427–434.

- 61. Gaval-Cruz M, Liles LC, Iuvone PM, Weinshenker D. Chronic inhibition of dopamine I2- hydroxylase facilitates behavioral responses to cocaine in mice. *PLoS One*. 2012; 7:e50583.
- 62. Soyka M, Rösner S. "Opioid antagonists for pharmacological treatment of alcohol dependence – a critical review". *Curr. Drug Abuse Rev.* 2008; 1:280–91.
- 63. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, Kim MM, Shanahan E, Gass CE, R o w e C J, G a r b u t t J C. "Pharmacotherapy for Adults with Alcohol Use Disorders in Outpatient Settings".Journal Am. Med. Assoc. 2014; 311: 1889–1900.
- 64. Mason BJ, Heyser CJ. "The neurobiology, clinical efficacy and safety of acamprosate in the treatment of alcohol dependence".Expert Opin. Drug Saf. 2010a.**9:** 177–88.
- 65. Mason BJ, Heyser CJ. "Acamprosate: A prototypic neuromodulator in the treatment of alcohol dependence".Central Nervous Syst. Neurological Disorders Drug Targets. 2010b; 9: 23-32.
- 66. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Rösner S, ed. "Acamprosate for alcohol dependence".Cochrane Database of Syst. Rev.2010; 9: CD004332.

