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RESEARCH ARTICLE

SACHET AND SMALL-VOLUME ALCOHOLIC/NON-ALCOHOLIC BEVERAGES IN NIGERIA – AN ABUSE AND TOXICITY RISK SURVEY

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ABSTRACT

Alcohol and substance abuse in Nigeria is fast becoming a public health menace. The unregulated proliferation, sale and consumption of low-price sachet and other low-volume alcohol has accentuated the incidence of alcohol abuse in the country. The potential risks associated with this scenario are further aggravated by the habit of including medicinal plant extracts locally believed to have physical or sexual vitality-enhancing property in many of these alcoholic/non-alcoholic liquid brands. Despite the increasing prevalence of this problem and its attendant physical, mental, and social health impact, there has not been any scientific report specifically focused on the variety and the chemical constituents of these low-cost brands in the country. The aim of this study, therefore, is to know the variety of the liquid brands available in major Nigerian cities, profile their chemical compositions – especially their alcohol and the medicinal extract contents. Surveys were carried out on convenient days starting from September 2022 through March 2023 in randomly selected streets in Lagos, Ibadan and the federal capital territory, Abuja particularly market and motor park areas where alcohol-related activities were likely to be high. All sachet and other small-volume alcohol packaged brands encountered were inspected and relevant data such as brand names, name(s) and address(es) of the manufacturers/marketers, brand unit price(s), percentage alcohol content, inclusion or omission of medicinal extracts, and the presence or lack of the official (government) National Agency for Foods and Drugs administration and Control's (NAFDAC) approval were captured. The surveys encountered a total of seventy-five (75) alcoholic and non-alcoholic brands (See table below). All the survey brands, except one (Alomo bitters), are manufactured in Nigeria with over 90 percent of these brands are produced in the South-western region of the country. Most of these brands existed in both sachets and in small-volume plastic containers. The sachet brands' volumes ranged from 50 to 70 ml and sold for N30 to N70 per unit while the plastic container brands' volumes ranged from 80 to 125 ml and sold for N60 to N200 per unit. Eleven brands were stated as non-alcoholic (zero %). Of the rest 64 alcoholic brands, 54 had and 10 did not have their alcohol contents stated on their labels. The percentage (%) alcohol contents of the brands ranged from the minimum of 15% to the maximum of 45%. Over half of the brands exhibited high (more than 30%) alcohol contents. Two-thirds of the brands had about 60 different medicinal plant extracts and spices in various combinations, included in their contents. Only about 37 did but 16 brands failed to disclose their medicinal extracts on their labels. A significant proportion of brands contain a variety of plant extracts (Asimina triloba, Lanneawelwitschii, Picrasma excelsa, Reglisse (Liquorice), Gentiane jaune, Rhubarb root, Guarana, etc.), food preservatives (sodium benzoate, citric acid E330), additives (aspartame, acesulfame-k etc.), flavours, colourants (Allura Red, Tartrazine E102) and supplements (Taurine, caffeine). Some these substances have toxicity concerns. More than half of these alcoholic and non-alcoholic brands did not indicate any therapeutic uses for their products. For those that did indicate their beneficial uses, these include physical and sex-related vitality enhancement, and alleviation of low back ache or menstrual disorders. Only eight brands failed to showcase the official approval (NAFDAC licence) to operate. It is worthy to note that 10 of the 14 brands which failed to specify their medicinal plant extract constituents were among those brands exhibiting government (NAFDAC) licence. None of the brands listed any adverse effects against their products. Only 19 brands gave any form of general or specific warnings to those for whom their products are not recommended or are contraindicated. Potentially toxic chemical compounds such as plant-derived acetogenins, alkylated hydroquinones, Juniper berry, glycyrrizin, glycyrrhetic acid, quassin and neoaquassin; and food additives Allura Red, tartrazine, aspartame, Acesulfame-k, citric acid (E 330), caffeine, several synthetic colorants and flavourings are included in many of the brands. These findings show there is alcohol abuse risk in some Nigerian cities due to unregulated production, easy access and low cost of sachet and other small-volume packages. The %alcohol, some medicinal extract, and food additive contents of some of these brands may not be safe for continued public consumption. There is a need for greater supervision/regulation of the production, sale and consumption of sachet and other small-volume alcoholic packages on one hand and for more effective alcohol-related public health awareness campaigns on the other.

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INTRODUCTION

Drug or substance abuse is said to occur when drugs or any other psychoactive substances, including alcohol, are used to achieve high or good feelings or inflict self-harm, outside of medical or legal prescription (1). Alcohol has been in widespread use in most parts of Nigeria – with the prevalence of its use reaching as high as 60 percent amongst the populace in some communities (2)(3). Hitherto alcohol used to be packaged, sold, and consumed only in big-volume bottles as beer and hot drinks; and alcohol use was restricted to beer parlours, restaurants, and private homes in Nigeria. Subsequently, there emerged the practice whereby alcohol, energy drinks and beverage laden with “aphrodisiac”/ “tonic” medicinal plant extracts began to be packaged in sachets and other small-volume containers. These alcoholic and non-alcoholic drinks are often seen openly displayed on the major streets – most commonly around motor parks and markets – of Nigerian cities, particularly, in the Southern regions and Abuja - the nation’s capital territory. Reasons commonly given by the habitual consumers of these beverages – most of whom are youths and male- include the need to feel “good,” “high” and “strong”; sexual vitality enhancement; and for the alleviation of chronic low back aches and/or pile. This situation of unrestricted alcohol access invariably implies alcohol abuse may in no time, if not already, become Nigeria’s leading public health menace with consequences that are better prevented than solved. Reports indicate alcohol abuse is associated with increased indulgences in multi-drug and multi-substance abuse, risky sexual behaviours, criminality, physical and mental health risks (3)(4)(5)(6)(7)(8)(9)(10) as well as emergence of various chronic organ (heart, kidney, liver and metabolic) diseases (11).

The risks associated with alcohol abuse risks in Nigeria are believed to have been accentuated with the introduction of packaged sachet alcoholic drinks into the public space similar to what was as seen in other African countries – Kenya (12), Malawi (13) and Uganda (14) – where production of low-priced sachet alcohol led to the worsening of the countries’ alcohol abuse. The risk drivers in Nigeria, just as in those countries, include unrestricted availability and sale of low-priced alcohol sachets and other low-volume alcohol packages – thus, making them freely accessible to, and affordable, by most members of the public including students and teenagers (1)(2)(3). Adding to these is the fact that many of these beverages contain extracts of medicinal plants some of which may have safety (toxicity), and/or addiction (abuse) concerns that may neither have been adequately addressed during their production nor highlighted on the products’ labels (4)(5). Another factor promoting abuse of most of these sachet and other small-volume alcoholic/non-alcoholic beverages is the practice whereby the producers give their brands names (e.g., Rokat bitters, Stone bitters, Action bitters, Horse-power bitters, etc.) which suggest the possession of sexual/physical vitality enhancing properties on one hand, and the inscription of ‘tonic’ and ‘aphrodisiac’ benefits/indications on the products’ labels on the other. Perhaps, the strongest factor driving the abuse of these alcoholic/non-alcoholic beverages is also the twin issue of rapid rate of their proliferation and of pervasive buzz of print, billboard and electronic advertisements promoting their illicit sexual and physical vitality enhancing benefits that remain largely unproven. Media reports indicate Nigeria’s food and drug regulatory body, the National Agency for Foods and Drugs (alcohol, inclusive) Administration and Control (NAFDAC), worried by the spate of, and in an attempt to scale down, the proliferation and the potential dire public health complications – namely; increased criminality, negative physical/mental health impact, increased mortality, poor educational and poor social responsibility performance indices- associated with widespread consumption of these alcoholic and non-alcoholic beverages, has in recent times recommended stoppage of new brand registrations. But despite the stakeholders’ acknowledgment of the widespread proliferation and abuse of these beverages even with the attendant adverse health and socio-economic consequences, there has not been any scientific report (as far as our literature search is concerned) specifically focusing on the variety of existing brands and their

chemical compositions. The aim of this survey, therefore, is to identify the variety of these brands existing in the public space in selected Nigerian cities, as well as highlight their percentage alcohol contents, the safety or otherwise of their medicinal plant extracts and food additive with a view to gauging the toxicity/abuse potentials of these constituents – and by extension, the beverages containing them.

METHODOLOGY

Some major Nigerian cities – Lagos, Ibadan, and Abuja - were randomly selected for this survey which lasted from September 2022 to March 2023. Streets, markets, and motor park areas in these cities where alcohol-related activities were likely to be high were randomly selected into the study and visited on convenient days. All sachet and small-volume alcohol and energy drink brands on display at sites of visit were inspected. Data such as the chemical constituents (particularly, alcohol, food additive, and medicinal plant contents), the package mode, the unit prices of the brands, the volumes of the different packages, the names and addresses of their producers/marketers, presence or lack of use guidelines, presence or lack of government’s (NAFDAC’s) approval, therapeutic indications (if any), and warnings on the brands’ labels were recorded. Samples for each brand were purchased. Internet Scientific searching platforms were used to search for the toxicity and abuse potentials of the various chemical components identified in the different brands. Data and information gathered were tabulated as below.

RESULTS

Survey outcome: A total of seventy-five (75) drink brands were encountered in the survey (See table below). Sixty-four (64) were alcoholic and nine (11) were not-alcoholic (% alcohol content). Most of these brands were packaged in both sachets and in small-volume (plate I and II) plastic containers. All the survey brands, except one (Alomo bitters), are manufactured in Nigeria with over 90 percent of these brands are produced in the South-western region of the country. The sachet brands’ volumes ranged from 50 to 70 ml and sold for N30 to N70 per unit while the plastic container brands’ volumes ranged from 80 to 125 ml and sold for N60 to N200 per unit. Of the 64 alcoholic brands, 54 did and 10 did not have their % alcohol contents stated on their labels.



Plate I. Some of the small-volume alcoholic brands encountered in the survey

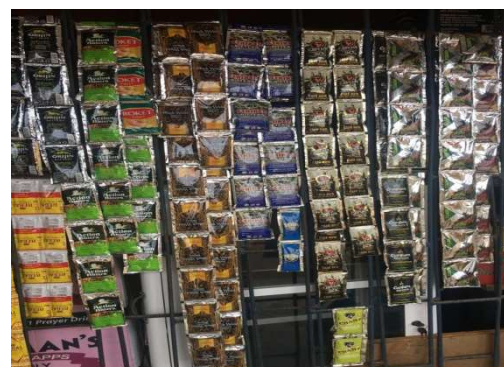


Plate 2. Sachet alcoholic beverages on open roadside display

The % alcohol contents of these brands inspected varied from the minimum of 15% to the maximum of 45% alcohol content. Two-thirds of the brands had about 60 different medicinal plant extracts and spices in various combinations, as parts of their contents – with only about 37 of them having their extract contents specifically shown on their labels while about 16 brands failed to disclose their medicinal plant components. A significant proportion of brands contain a variety of plant extracts (Asimina triloba, Lanneawelwitschii, Picrasmaexelsa, Reglisse (Liquorice), Gentiane jaune, Rhubarb root, Guarana, etc.), food preservatives (sodium benzoate, citric acid E330), additives (aspartame, acesulfame-k etc.), flavours (Orange, melon) colourants (Allura Red, Tartrazine E102) and supplements (Taurine, caffeine). More than half of these alcoholic and non-alcoholic brands did not indicate any therapeutic uses for products. For those that did indicate their beneficial uses, the most frequent uses include physical and sex-related vitality enhancement, and alleviation of low back ache, pile, or menstrual disorders. Only ten brands failed to showcase the official approval (NAFDAC licence) to operate. It is worthy to note that 10 of the 14 brands which failed to specify their medicinal plant extract constituents were among those with government (NAFDAC) licence. None of the brands listed any adverse effects against their products. Only 2 brands gave directives on how to use their products. Only 19 brands gave any form of general or specific warnings to those for whom their products are not recommended or are contraindicated. Some of the plant extracts and food additives have toxicity and abuse/addictive potential. Integrated taxonomic information system (ITIS) botanical identification of the extracts in the drink brands indicate the medicinal plants belong to the following classes - Magnoliopsida 94%, Angiospermae, Liliopsida, and Pinopsida 2% each, and the following families – Fabaceae 11.5%, Apocynaceae and Annonaceae 7.7% each, Areaceae and Rubiaceae 5.8%, Spinaaceae, Lamiaceae, Meliaceae, Simaroubaceae, Lauraceae, Apiaceae, Rutaceae, Asteraceae, and Clusiaceae 3.8% each, and Combretaceae, Cappaceae, Acoraceae, Gentianaceae, Zinzigeraceae, Polygoraceae, Poaceae, Alliaceae, Moringaceae, Aloaceae, Andardiaceae, Zinzigeraceae, Cupressaceae, and Analiaceae 1.9% each. Further literature search indicates some potentially toxic chemical compounds such as plant-derived acetogenins, alkylated hydroquinones, Juniper berry, glycyrrizin, glycyrrhetic acid, quassin and neoquassin; and food additives Allura Red, tartrazine, aspartame, Acesulfame-k, citric acid (E 330), caffeine, several synthetic colorants and flavourings are included in many of the brands.

DISCUSSION

The thrust of this study is to draw the attention of the relevant stakeholders to the potential public health menace inherent in unrestricted production, sale, and consumption of alcohol-based and non-alcoholic sachet or low-volume beverages. More so when several of such drinks are commonly mixed with medicinal plant extracts and/or food additives the safety of which may not have been adequately addressed during production. Thus, the discussion of the findings of this survey will be to highlight the potential risks associated with the unwholesome manufacture and use of these beverages themselves, the various medicinal plant extracts and food additives included in them. From our survey, a quick perusal will show the proliferation of these brands may be related to the fact that some of the producers of these brands manufacture up to four or five products apiece, under different names, with little or no differences in their contents. This practice ensures uninformed consumers of these beverages are exposed to the risk of additive alcohol intoxication and/or additive toxic medicinal extract/food additive effects resulting from multiple picks of different brand products from the same producer. Another factor worthy of attention is the high alcohol contents of the brands under the current study, with more than half of the surveyed beverages exhibiting alcohol by volume well over 30%. If the alcohol content of those brands which disclosed their alcohol content could be this high, the high level of the ten brands which chose not to disclose their alcohol contents is left to the imagination. These aforementioned factors coupled with the accessibility/affordability and the incessant promotional adverts of these brands engender continued consumption of these brands.

Long-term alcohol abuse has been linked to increased disease morbidity/mortality, poly drug/substance abuses, crime rates, and poor social responsibility (2)(6)(8)(9)(10)(11)(12)(13)(14). The highlighted gaps in the production, sale, and use of alcohol in the country calls for greater regulation alcohol use in the country. The desirable measures should include restriction in the registration of new producer companies, immediate and outright banning of sachet and small-volume alcohol packages, proscription of alcohol-related advertisements, limiting percentage alcohol contents in these brands and increasing health awareness campaigns on the negative impacts of alcohol abuse.

The inclusion of medicinal plant extracts traditionally known or suspected to have health/sex enhancing properties in these beverages is quite rampant and increasing because of the expected “tonic” / “aphrodisiac” benefits associated with the consumption of these brands. This unwholesome practice puts the public at risks of toxicities that may be inherent in these medicinal extracts. In our survey, of about fifty-four brands that have one or more plant extracts included in them about 12 did not disclose their extract contents, thus, exposing consumers to potential toxic effects of these plants. Literature scrutiny of the medicinal plants from which the extracts in the beverage brands are gotten shows some of them possess toxicity/abuse liabilities that may endanger their consumers especially on a long-term basis. So, the rest of this discourse will only highlight those extracts – and subsequently, those food additives and preservatives which may one or the other abuse/toxicity concern. Two of the medicinal plant extracts included in one of the brands encountered in this survey are potentially toxic to consumers especially if exposed to them over a long period.

Previously, acetogenins derived from the Asimina triloba fruits have demonstrated neurotoxicity in animal (15)(16) and alkylated hydroquinones derived from Lanneawelwitschii have been found cytotoxic in human (17) (18) studies. Panax ginseng is a widely used adaptogenic plant long viewed to be largely safe but has lately been a subject of safety reassessment. This extract has demonstrated abuse and cytotoxicity liabilities in both animal and human experiments (19)(20). Juniper berry – obtained from Juniperus communis L. - is one of the constituents of an ‘aphrodisiac’ brand we came across in this study. Only minute daily amounts (1-6 g) of this berry are now recommended due to the fact that immunotoxic, abortifacient, and nephrotoxic adverse drug effects have been reported for its supplements (21)(22). Compounds isolated from Coriander (*Coriandrum sativum*) – an extract component of one of the brands seen in this survey are suspected to be toxic to humans judging from some animal studies (23) Reglisse (Liquorice) (*Glycyrrhiza glabra*), indicated as one of the components of one of the beverages in this study, is a commonly used traditional alleviation of multiple diseases. However, research indicates extracts from this medicinal plant may have abuse and toxicity drawbacks which are viewed to be linked to the hitherto largely overlooked extensive enterohepatic circulation of its glycyrrizin and glycyrrhetic acid compounds (24)(25)(26)(27). Picrasmaexelsa, listed as a constituent of one of our survey findings, has quassinoid compounds: quassin and neoquassin which exhibit significant inhibitory interactions with cytochrome P450 (CYP) enzymes (28). This has raised safety red flags concerning long-term use of this plant extract, especially when consumed in high quantities. Picralima nitida, a member of the Apocynaceae, is listed in our findings as a component of one of the brands. Studies have found extracts of this plant to be potently genotoxic, glutathione-depleting, hepatotoxic, nephrotoxic, and teratogenic (29)(30). Due to findings such as this, caution is therefore recommended for its use generally, and it is advisably contraindicated in pregnant women. Saponins from *Massularia acuminata* stem extracts in high doses have been shown to be potentially toxic on the male reproductive system in rats (31). *Massularia acuminata* is one of the medicinal plant extracts included in some of the alcoholic brands in this survey. Glycosides isolated from *Fadogia agrestis* roots have been found to be cytotoxic on certain bacteria and parasites, and injurious to rodent liver and spleen (33)(34). Cassia cinnamon has been shown to contain high amounts of coumarins which have been found to be

Table of list of alcoholic/non-alcoholic beverages in selected Nigerian cities

Serial no.	Brand names (Manufacturers/ Marketers)	Alcohol (%/Vol.) & other chemical contents	Stated benefits/uses	NAFDAC 's licence	Stated adverse effect(s)/ contraindications
1	Action bitters (International distillers, Ota, Ogun State, Nigeria)	40% Symphonia globulifera, Carcinia kola, Tetrapleura tetraptera, Lanneawelwischii, dimeralised water, ethyl alcohol, colours, E150(a), Brandy flavours	“Action”	Present	Nil Nil
2	Kakaraka bitters (BEND Industries, Ugbe, Ondo State, Nigeria)	40% *Unspecified herbal extracts, ethanol, water, caramel	Energy boost Vitality Strong erection Body pain relief	Present	Nil Nil
3	Igboya bitters (Eastwood Edwin Russ & Food Distilleries Ltd. Ikorodu, Lagos, Nigeria)	30% Treated water, food grade spirit, honey, Caramel, Asimina triloba, Cocos nucifera, Allium sativum, Alstoniaboonei, Citrus aurantifolia, Vernonia amygdalina, Zingiber officinale, Aloe bardensis, Butterscotch extractflavour	‘Enhanced manpower’	08-6264	Nil Nil
4	Jagaban alcoholic drink (akaKick, Manpower) (TT Ltd Akure, Ondo State, Nigeria)	% alcohol content unspecified Ginger, ginger flavour, treated water, caramel, ethanol (written as Enternal)	Manpower	Not stated	Nil Nil
4	Old port coffee flavoured liquor (Bramraj Food & Beverages Ltd. Ogere, Ogun State, Nigeria)	30% Water, undenatured ethyl alcohol, sugar, coffee flavour and caramel	None	08-6489	Nil Nil
5	Erujeje ginger flavour liqueur (Bramraj Food & Beverages Ltd. Ogere, Ogun State, Nigeria)	42% Waler, undenatured ethyl alcohol, sugar, coffee flavour and caramel	Not specifically stated	08-1241	Nil Nil
6	Alogin power alcoholic drink (Peace Standard Pharmaceutical Ltd. Ilorin, Kwara State, Nigeria)	35% Korean ginseng, sucrose, citric acid, caramel, Allura Red, sodium benzoate, ginger flavour, ethyl alcohol, treated water	Not expressly stated. (Sex or health enhancement inferred by the label word ‘POWER’ boldly written and a drawing of a male and female in a romantic posture on the plastic package)	A8- 1714L	Nil Nil
7	Seaman’s Schnapps (Nigera Distilleries Ltd. Sango Ota, Ogun State, Nigeria)	40% Treated water, Schnapps flavour, ethanol	Nil Stated	01-1492L	Nil Nil
8	Striker Bitters (SHASH Industries Ltd, Sango Ota, Nigeria)	35% *Unspecified root extracts, treated water, ethanol, Flavour	Unspecified	08-1338	Nil Nil

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9	Squadron alcoholic drink (Intercontinental Distillers, Ota, Ogun State, Nigeria).	42% Demineralised water, ethyl alcohol, Rum spirit, Sugar, Colouring E150 (a)	Not Stated	01-1573L	Nil Nil
10	Chelsea London Dry Gin (Intercontinental Distillers, Ota, Ogun State, Nigeria)	43% Demineralised water, Ethyl alcohol, Gin flavour, Juniper berry extract	Not stated	01-1572L	Nil Nil
11	Predator energy drink (Nigeria bottling Company Ltd. Iddo, Lagos, Nigeria)	Zero % Carbonated water, sucrose, citric acid, tartaric acid, sodium citrate, pineapple & vanilla flavours, taurine (100 mg/100 ml), potassium sorbate, sodium benzoate, caffeine, sulfite ammonia caramel, vitamins B3, B6, inositol (1 mg/100 ml)	Vitality and freshness	A8-5136	Nil Warning of high caffeine content, not recommended for children, pregnant & lactating women, caffeine-sensitive persons, diabetics. Further warning to drink responsibly to a limit of 1 predator bottle a day and not to mix with alcohol.
12	Yaahu Gin (Bramraj Food & Beverages Ltd Ogere, Ogun State, Nigeria).	30% Contents not clearly stated	Not stated	Nil	Warning statement of alcoholic drinks being injurious to health is inscribed on the product label
13	Gbe see fire ginger drink (CHUBY-ZION IND. NG. LTD. Orile Ifo, Ogun State, Nigeria)	30% *Unspecified herbal extracts, water, ethanol, ginger, caramel,	Not stated	A8-8318L	Nil Nil
14	Palm wine native gin (ThonyKalyst Ltd, Ado-Ekiti, Ekiti State, Nigeria).	30% Refined palm wine and water	Not stated	Not seen	Nil Nil
15	PASA-BITTERS (IKI LEADS NIG. LTD. Atan, Ogun State, Nigeria)	40% *Unspecified plant/herbal extracts, Ethanol, caramel, Treated water.	Appetizer Male vitality	A1-9982L	Nil Nil
16	DeRok quality café liqueur (Intercontinental Distillers, Ota, Ogun State, Nigeria)	40% Demineralised water, Sugar, Rum spirit, Ethyl alcohol, colouring, E150 (a), Café extract, Cream flavour	Not stated	A1-9202L	Nil Nil
17	Jekomo herbal mixture (Victoria Adeyinka Nig. Enterprises, Ibadan, Oyo State, Nigeria)	Zero % Aristolochiaringes, Curculiga Pilosa, Phyllanthus amarus, Burantashi, Caramel	Male sex enhancement Pile Waist pain Low sperm count	A7-2929L	Nil Consumers warned not to take in pregnancy
18	Black wood alcoholic bitters (Bramraj Food & Beverages Ltd Ogere, Ogun State, Nigeria).	40% Water, caramel, Undenatured Ethyl alcohol, plant extracts (Quassinoids, glycerine)	Nil stated	B1-7530L	Nil Nil
19	Captain Jack blended café rum. (Sollar1, Cocoa Industries Road, Ikeja, Lagos, Nigeria)	37.5% Demineralised water, ethyl alcohol, caramel, sugar, coffee extract and rum concentrate	Not stated	08-2309L	Nil Nil

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20	Orijin bitters (Guinness Nig. Plc, Ikeja Lagos, Nigeria)	30% Neutral alcohol, caramel, citric acid, trisodium citrate, sugar, chamomile, thyme, cinnamon extracts	Not stated	08-0630	Nil
21	Get alert liquor 'Power Booster.' (R. N. Tobex Resources Ltd. Sango Ota, Ogun State, Nigeria)	27.5% De-ionised water, ethanol, gelatin, milk, sugar & vanilla	Energy boost	08-59511	Nil Nil
22	Bull London dry gin (Intercontinental distillery ltd, Sango Ota, Ogun State, Nigeria)	% alcohol content not declared De-mineralised water, ethyl alcohol, coriander extract, gin flavour,	Nil	01-9828	Nil 18+ Warning
23	GbesegberaAgbo Cleanser (CHUBY-ZION IND. NG. LTD. Orile Ifo, Ogun State, Nigeria)	32% Composition not shown. *Un specified medicinal extracts blended	Vitality, Manpower	A8-5763L	Nil Nil
24	Champ premium dry gin (Shiashi industries ltd. Ota Ogun State)	43% Water, Ethanol, flavours	Nil	BL-5929L	Nil Nil
25	Power bitters (original alcoholic bitters) (Euro Global Foods & Distilleries Ltd., Sango Ota, Ogun State, Nigeria)	35% Ethyl alcohol, demineralized water, herb extracts [Gentiane jaune (Gentiane lutea), Quiriquinia (Cinochonapubscens), Reglisse (Glycuchirza glabra), orange juice (Citrus aurantifolia, Picrasmaexcelsa, bitters and caramel	Nil	08-1527	Nil Nil
26	Ogoro native gin (Success Star Global Services Ltd. Lagos, Nigeria)	% alcohol content declared Treated water, Raffia palm spirit.	Nil	A8-4139L	NilNil
27	Riverine native gin (IKI LEADS LTD, Atan, Ogun State, Nigeria)	40% Other chemical components not stated	Nil	A8-5554L	Nil Nil
28	Cheezo Africa liquor drinks (a.k.a. Baba 70). (Cheezo Enterprises, Ejigbo Lagos, Nigeria)	% alcohol not declared *Plant extracts, caramel, ethanol, honey, lemon.	Men power, Pile, Stomach pain, Toilet infections, Body & waist pain	B1-8288L	Nil Nil
29	Best liqueur cream (Best Global Brands Ltd. Ogba Ikeja, Lagos, Nigeria)	17% Cream concentrate, water, ethanol, malt, whisky, marula flavour, maltopectin sugar.	Nil	08-3127	Nil
30	Mee Makossa schnapps (Conglome ventures ltd, Ipaja, Lagos, Nigeria)	38% Treated water, schnapps flavour, ethanol	Nil	08-2227L	Nil

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31	DOET cream liquor (DOET Nig. Ltd. Akure, Ondo State, Nigeria)	35% Milk cream, gin, gin flavour, sugar, spirit	Nil	A8-0809	Nil
32	Horsepower bitters(thonykalyst Nig. Ltd. Ado- Ekiti, Ekiti State, Nigeria)	42% Herbal extracts, purified water, ethanol, flavours	Sex enhancement	08-7293L	Nil Nil
33	Jedi oloyin alcoholic drink (Bend Diamond estate, Lagos, Nigeria)	33% Natural honey, Moringa oil, seed & leaf	Pile, Weak penile erection, Back pain, Stomach problems	A8-2678L	Nil Nil
34	Spena whisky (Chubby Zion Industries Ltd. Ore road, Ondo State)	30% Demineralized water, ethyl alcohol, whisky flavours	Nil	A8-6321L	Nil Nil
34	Odogwu bitters alcoholic drink.(IKI LEADS NIG. LTD. For Cubana Investments Co. Ltd. Victoria Island, Lagos, Nigeria).	30% *Unnamed selected African herbs, ginger, honey,	Nil	08-3849L	Nil Nil
35	Buga alcoholic bitters (Success Star Global Services Ltd. Diamond estate, Lagos, Nigeria)	19% *Herbal extracts, treated water, ethanol, caramel, Azadirachta indica	Nil	A8-3907L	Nil Nil
36	Ijaaw dry gin (highstar Distilleries Ltd. Ikorodu, Lagos, Nigeria)	33% *Other chemical components not stated	Nil	A8-3987L	Nil Nil
37	Colidonsvarca dry gin. Eastern Distilleries & Foods Ltd. Onitsha, Anambra State, Nigeria)	43% Treated water, food grade ethanol, gin flavour	Nil	01-7557	Nil Nil
38	Amotekun Herbal Bitters (Paronih Trading Ventures. Ibadan, Oyo State, Nigeria)	% alcohol contentnot declared Portable water, Zinziger officinale, Picralimaniltida, Massularia acuminata, citrus x limon, Aloe barbadensis Miller, Fadogiaagrestis	Nil, but aphrodisiac effect suspected by the reason of the product's label picture	2577085	Nil Nil
39	Gbemidebe herbal mixture. (TT LTD. Ijoka road, Akure Ondo State, Nigeria)	*Percent alcohol and other chemical contentsnot declared	Manpower,Pile, waist pain, low sperm count	A8-0909L	Nil 18+ warning
40	Japata alcoholic bitters (aka 100% minister of enjoyment) (Chigodson Int'l Co. Ltd. Isheri Oshun Lagos, Nigeria)	30% Caramel, ethanol water, herbal extracts (Angelica archangelica, Cassia cinnamon, Rhizome	Not expressly sated but suggestive of good pleasure	08-2294L	Nil Nil
41	Shana woleoko-jedi alcoholic drink (tofmaltofem Limited.Ijoka road, Akure Ondo State, Nigeria)	35% *Other chemical components not stated	Energy boost (vitality), Immune system booster, Man-power, pile, waist pain, quick ejaculation, menstrual pain	A8-0909L	Nil Nil
42	Ballamor bitters (Eastern Distilleries & Foods Ltd. Onitsha, Anambra State, Nigeria)	25% Caramel, food grade ethyl alcohol, *unspecified root extracts, deionized water	Nil	B1-4087	Nil Nil
43	Regal London dry gin (Marketed by Grand Oak Ltd. Lagos State. But produced by Nigeria Distilleries Ltd. Ogun State, Nigeria).	43%Ethyl alcohol, ginflavour, extracts (Juniper, lime & caraway), water	Enjoyment	Not stated	Nil Nil
44	Olekoko traditional Herbal mixture (aka, Ason bitters, oshaprahprah)(Ajebi traditional Company.Owode, Oyo, Oyo State, Nigeria)	Zero %Aloe vera root & leaf, caramel herbal flavour extract, Ivorensis (khaya), Rhuharb roots, Senna leaf, water	Energy booster, blood booster, menstrual disorders	A7—2993L	Nil Nil
45	Passion energy drink (Marketed by Orange Drugs Ltd)	Zero %Ginseng, taurine, caffeine, inositol, nicotinamide, vitamin B1, vitamin B6,aspartame, acesufam-k, coffee, maltol, anhydrous citric acid, effervescent soda 12, melon flavour(76860-31), orange flavour 76905-71, guarana, flavour 1244-32, sugar flavour 532-00024-17, maltodextrin, sodium bicarbonate.	Energy with extra passion	01-8933	Nil Caution for persons with caffeine allergy. C/Is: Pregnant women, children

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46	Baby oku De Man-power alcoholic bitter drink. (Chuby-Zion Ind. Nig. Ltd. Ifo, Ogun State, Nigeria)	42%Water ethanol, caramel, herbal extracts (Angelica root, Cassiasenna leaf, Rhubarb root & Aloe)	Not expressly stated but aphrodisia implied by its nomenclature	B1-4103L	Nil Nil
47	Bajinotupoka alcoholic herbal drink (Seakam Global Resources Ltd. Ibadan, Oyo State, Nigeria)	37%*Natural herbs, caramel, saw palmetto, ethanol, treated water	Energises immune system.Relieves waist Relieves menstrual pain	08-5354L	Nil 18+ warning Drink responsibly warning
48	Tombo bitters (Agrim International FZE. Calabar Cross River State, Nigeria)	% alcohol contentnot declared Ethyl alcohol, De-mineralisedwater, herbal extracts: Garcinia kola, lemon grass, mint, Tetrapleuratetraptera	Nil	08-9476L	Nil Drink responsibly warning.
49	Tombo Vodka (Agrim International FZE. Calabar Cross River State, Nigeria)	42.8%Demineralised water, neutral alcohol	Nil	08-2659L	Nil Drink responsibly warning
50	Zazoozehh alcoholic bitters (Big Twins Global Concept. Iwo road, Ibadan, Oyo State, Nigeria).	35%Distilled water, Musa paradisiaca, Diocleareflexa	Nil	04-8328L	Nil 18+ warning Drink responsibly warning
51	Stone herbal non- alcoholic mixture(Odadest companyIdi Ayunre Ibadan, Oyo State, Nigeria).	Zero %Terminalia laxiflora, Zingiber officinale, caramel syrup, treated water	Benefits:Boost men's sexual performance, relieves impotence, firm & strong erection, increases ejaculation & libido, cures low sperm count, infection & syphilis. Prevents typhoid fever, menstrual pain, pile & back pain.	A7-4066L	Nil Nil
52	Okokoriko herbal bitters. (ashifaulhaqi Ltd.Ibadan, Oyo State, Nigeria)	Zero %Hunteriaumbrellata, licorice, caramel (sugar base), water	Man's extra power, pile, waist pain, increases sperm count & quality, treats women fertility.	Not stated	Nil Not to be taken by pregnant women
53	Rocket ginger liqueur(Intercontinental distilleries Ltd.Ota Ogun State, Nigeria)	30%Dimineralised water, ethyl alcohol, ginger extract, sugar, colour: E150(a), ginger flavour.	Nil	01-9885L	Nil Nil
54	Champ ginger flavoured spirit drink.(Shiashi industries ltd 50, Geri Road, Ota Ogun State, Nigeria)	30%Ethanol, water, ginger extract	Nil	A8-5187L	Nil Nil
55	Cremica liqueur (Agrim International FZE. Calabar Cross River State, Nigeria)	15%Alcohol, demineralized water, condensed milk (milk, sugar, water), chocolate flavour.	Nil	A8-7414	Nil Drink responsibly warning

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56	Fearless energy drink (Rite Foods Ltd Shagamu-Benin road, Ogun State, Nigeria)	Zero %Water, sugar, carbon dioxide, citric acid (E 330), preservatives potassium sorbate (E202) and sodium benzoate (E211), flavouring, acidity regulator sodium citrates (E331), taurine, caffeine (0.031%), inositol, niacin, colours tartrazine (E102) and sunset yellow (FCF E110), extract de ginseng, Vitamin B6, vitamin B12.	Vitality	08-6116	Nil High caffeine content alert Not recommended for children, breastfeeding and pregnant women
57	Kabiyesi alcoholic bitters ginger drink (Eastwood Edwin Russ Distilleries & Foods Ltd. Ikorodu Lagos, Nigeria)	30% Treated water, Food grade ethanol, honey, caramel, ginger, plant extracts (Lecaniodiscus (cupanioides)).	Nil	08-5912L	Nil 18+ warning
58	My Boo bitters herbal alcoholic drink (IKI LEADS NIG. LTD. Atan, Ogun State, Nigeria)	40% Ethyl alcohol, water, Bitter extract, caramel, Ocimumgratissinum,flavours	Nil	08-3849L	
59	Ji maasunginger+garlic drink (Westview distilleries Nigeria. Km 41, Ofada, Mowe, Ibafo-Ibadn Express Way, Ogun State, Nigeria).	42% Food grade spirit, treated water, caramel, honey, plant extracts: Allium sativum, Zinzigerofficinale, &Xylophia aethiopia	Reduces muscle pain & nausea sickness. Reduces internal burns. It is antioxidant. Reduces blood sugar, indigestion, stomach discomfort& excess cholesterol level. It improves memory loss & promotes longevity. It boosts immunity & reduces risk of hear attack. It enhances performance & purifies blood.	08-5578L	Nil Drink responsibly & +18 warning seen
60	Giantmansamarina blended dry gin(Samanna Foods Ltd. Ndemli North L.G.A., Anambra State, Nigeria)	43% Ethanol, water, gin flavour	Nil	A8-1436	Nil Nil
61	Amber energy drink (Amber Drinks Ltd. Ikeja, Lagos, Nigeria)	Zero % Water, sugar, citric acid, E330, carbon dioxide, sodium citrate, E331, caffeine (32/100ml), glucose-fructose syrup, taurine, inositol, colours, ammonia caramel, e150c, riboflavins, E101, flavouring, niacin, pantothenic acid, vit. B6, B12, guarana.	Improves alertness. Stimulates metabolism. Improves concentration. Reduces fatigue.	E1-1047	Nil Nil
62	Squad 5 blended dark rum	45%Treated water, ethanol, sugar syrup, caramel,	Nil stated	01-4844L	Nil Nil
63	Coco samba milk &chocolate drink with herbal ingredients(Bullion Go-Neat Global Limited, Km 36, Lagos-Ibadan Express Way, Ogun State, Nigeria).	Alcohol % not declared. Water, Aloe vera, caramel	Nil stated	A8-9149	Nil Nil

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64	Alomo bitters (Kasapreko Company Limited. Accra, Ghana)	40% Purified water, alcohol, plant extracts (Khaya senegalensis, Mondia whitei, Capparis erythrocarpus)	Not stated	Not declared	Nil Drink responsibly warning
65	Oloyoherbal bitters alcoholic drink (DR NWAKOR'S 7 KEYS NIG. LTD. Badagry, Lagos, Nigeria).	40% Treated water, caramel, Azadirachta indica, Calamus rhizome (Acorus calamus), ethanol.	'Manpower' Waist pain Fat burning	08-0857L	Nil Drink responsibly warning
66	(Daboo herbal bitters. Ibadan, Oyo State, Nigeria)	Zero % *Other contents not stated	Nil	Not declared	Nil Nil
67	Lacoco liqueur (Vodka & berry blended drink)(Sunlight Food Industries Limited, Isheri, Ogun State, Nigeria)	42% De-ionised water, sucrose, citric acid, sodium citrate, pantothenic acid, vitamins B6, B12, vodka, flavouring	Nil	08-8542L	Nil Drink responsibly warning seen
68	Original s'enuebo (Success Star Global Services Ltd. Diamond estate, Lagos, Nigeria).	% alcohol not stated *Herbal extracts, water, ethanol, honey, etc.	Waist pain Stomach pain 'Manpower' Menstruation pain Rheumatism Pile	A8-1173L	Nil Stated Contraindicated in pregnant women
69	Small Body Big Engine Bitters. (Chuby Zion Nig. Ind. Ltd. Ifo, Ogun State, Nigeria).	20% *Herbal extracts, treated water, ethanol	Cure of all types of pile, weak erection, back pain, stomach problems, manpower, menstruation problems and rheumatism	08-6612L	Nil Stated Drink responsibly warning seen
70	Ghan natural native gin (aka Original Ghana drink) (Chuby-Zion Ind. Nig. Ltd. Ifo, Ogun State, Nigeria).	30% Water and ethanol	Not stated	A8-5574L	Nil +18 warning
71	Blended Hisky alcoholic drink (Salight Food Industries Ltd. Isheri, Ogun State, Nigeria)	% alcohol not stated Water and ethanol	Nil	08-8536L	Nil Nil
72	De-Marshall Whiskey SBA Marshall Ventures. Ibadan, Oyo State, Nigeria)	% alcohol not stated Water and ethanol	Nil	Nil	Nil Nil
73	Gbera (ennyrehoboth globalventure (Ibadan, Oyo State, Nigeria)	Zero % Khaya gradifoliola, Mangifera indica, Alstonia boonei & jollyanum	Pile Manpower STD Body & waist pain, etc. 2-4 table spoons daily	A7-4230L	Nil Nil
74	Gbabee (Enny Rehoboth Global Venture Ibadan, Oyo State, Nigeria)	15% *Herbal extracts Not disclosed	Manpower Pile Back & Waist pain	Not seen	Nil Nil
75	Museya bitter (Har-Rahman Khabul herbal, Nigeria Limited.)	Zero % Herbal contents not disclosed.	Pile Irregular menses Stomach disorder ½ bottle capful twice daily for children 1 capful twice for adults	Not seen	

potentially hepatotoxic and nephrotoxic in humans (35). Cassia senna L. and Rhubarb root extracts have been used as effective laxative but anthraquinones isolated from both plants have demonstrated significant hepatotoxic and nephrotoxic effects to warrant re-screening of their safety for chronic use (36)(37)(38). Guarana (PaullinacupanaKunth var. sorbilis (Mart.) Ducke) is a high caffeine-containing medicinal plant whose seed extracts have been traditionally used as stimulants. Its concurrent inclusion with caffeine in the same drinks could engender additive caffeine effect which may be injurious to health. The cytotoxic and addictive (abuse risk) effects of guarana have been shown to be directly related to its caffeine levels in the body. These levels are reportedly aggravated when guarana is combined with caffeine, or taurine, or both (39)(40)(41)(42)(43). Xylopi aethiopia is a medicinal plant with high nutritional value and efficacy in wide spectrum of diseases such as amenorrhoea, cough, malaria, uterine fibroid, and constipation. However, stem bark or fruit decoction and xylopic acid (a compound isolated from this plant) have been shown to be toxic to rat's reproductive system (44)(45). Low dose sub-chronic administrations of *Khaya senegalensis* extracts in rats have been associated raised hepatic enzymes – implying long-term use of this plant may be injurious to the liver (46)(47). Extracts from *Mondiawhitei* - a well-established aphrodisiac medicinal plant - have been reported to cause neurotoxic histological lesions in rat's brain. A chlorinated coumarinolignan derivative isolated from the plant is suspected to be causally linked to this toxicity (48)(49). Our other concerning findings in this survey include the fact that, beyond the mere mention of their names, specific parts of the medicinal plants included in the brands are not clearly stated; multiple medicinal plants with safety concerns are included in a brand, and generally adverse effect documentation is lacking on these plant extracts. Proper labeling of the plant part(s) used in the brands will give clearer catalogue of the anticipated adverse reaction(s) if any. From our literature review, it is obvious that, even beyond the manufacturers, vital scientific information is still unavailable regarding the safety profile of a lot of the medicinal plants (e.g., *Lecaniodiscus cupanioides*, *Dioclea reflexa*, *Terminalia laxiflora*, *Mondiawhitei*, etc.) in this study. Such knowledge gaps can only be shortened by rigorous animal and human toxicity studies by the Scientific world.

The realization that these alcoholic and non-alcoholic brands will be sold and consumed on a long-term basis makes the need to intensify research on their safety very imperative. The food preservatives/additives/flavours/colourants/supplements in our findings are numerous and include calamus rhizome, caffeine, taurine, citric acid, Allura Red, sodium citrate (trisodium citrate), tartrazine (E 102), aspartame, sunset yellow (FCF E 110), and different flavouring agents. The artificial flavours are brandy, butterscotch extract, ginger, coffee, caramel, schnapp, gin, vanilla, cream, marula, and chocolate. Because of their large numbers, only those with the most safety risks will be discussed any further. Calamus rhizome (*Acorus calamus*) is unique in being both a medicinal plant and a food additive. It is a substance that has been shown to produce hallucinogenesis via its *in vivo* generation of a mescaline-like biomolecule (48). Additionally, the β -asarones isolated from *Acorus calamus* have been reported to be potentially genotoxic, carcinogenic, and hepatotoxic (50)(51)(52)(53)(54)(55). Owing to these effects, the use of β -asarone-containing food additives like *Acorus calamus* has been either banned outright or restricted in climes like Europe. In the latter scenario β -asarone body limits have been pegged at 0.1 to 1.0 g/kg body weight (53). Now, an uninformed mind is liable to overlooking the potential toxicity inherent in this plant and food additive, but this risk can be screened out at the point of registration of the culpable brand by requisite technical competence at the level of the regulatory authorities to safeguard public health. Allura Red is a synthetic food colourant the chronic consumption of which reports indicate may be linked to increased incidence of gastro-intestinal tract-based immune inflammatory pathologies, childhood behavioural anomalies e.g., attention-deficit hyperactivity disorder (56)(57)(58). The popularly used sodium benzoate and potassium benzoate hitherto thought to be safe have both been found to exhibit some degree of genotoxicity to human lymphocytes *in vitro* studies (59)(60).

The chances of getting a positive mutagenicity if other body cells are chronically exposed to these same food additives, especially in high doses, are high. Taurine, the most abundant intracellular sulphur-containing essential amino acid of non-protein nature, is yet another commonly used food supplement by the manufacturer of energy/vitality drinks. This chemical biomolecule has always been viewed to play major and beneficial role in certain vital human pathophysiological processes such as homeostatic regulation of key body electrolytes, immunocompetence, inflammation, carcinogenesis, mental and cellular oxidative stress, epilepsy, mood disorders, and hyperactivity (61). However, the finding that its safety is unpredictable at the body concentrations higher than 3 g/kg and that it exerts inhibitory interaction on the vastly useful multi-xenobiotic metabolizing hepatic cytochrome P450 enzymes is drawing fresh concerns on the safety of this food supplement, especially when taken in high amounts on a long-term basis (62)(63). Caffeine, widely regarded as the most abused stimulant substance, is a frequent constituent of energy drinks. Its addictive property as well as its toxicities – including mood swings, insomnia, palpitations, and nervousness in consumers of caffeinated beverages have been well reported (64)(65)(66)(67)(68). Some other reports have also indicated that caffeine toxicities are aggravated further when used combined with alcohol (69). Compared to alcohol alone, consuming caffeinated energy drinks with alcohol is also associated with increased rates of excessive drinking, impaired locomotor skills, increased sexual behaviour, alcohol dependence and poisoning risks (68). In our survey, safety concerns should be raised over a particular energy drink brand which combines caffeine on its own merits with guarana – a plant with high caffeine content – thus, risking caffeine over-dose and toxicity. Research further indicates combining guarana with either caffeine or taurine increases the creation of an intracellular reactive oxygen species deficits that are associated with neurite degeneration and cytotoxicity (69)(70)(71). Greater scrutiny at the point of registration of such brands would have necessitated removal of the caffeine sources to forestall unintentional caffeine-related adverse events. The synthetic dipeptide non-nutritive high-intensive sweetener aspartame has been experimentally implicated in the causality of cellular oxidative stress, brain tumours, mood and cognitive derangements, whether administered at the normal acceptable daily limits of 40-50 mg/kg body weight or higher (72)(73)(74)(75)(76). The continued use of this food additive in an energy drink in our country puts the health of the public at risk and calls for greater toxicity screening by the relevant stakeholders at the point of product registration. Acesulfame-K is another non-nutritive high-intensive artificial sweetener that has been equally associated with increased risks of genotoxicity (76).

Maltodextrin included in one of the brands of this survey is a simple sugar liable to generating exaggerated immediate postprandial hyperglycemia (77). Maltodextrin's high glycemic index may constitute significant health risk (obesity, diabetes mellitus, hypertension, etc.) in the long-term consumption of this beverage. The usage of complex (e.g., isomaltose) (78) as opposed to simple carbohydrates should be recommended by the regulatory bodies to the manufacturers of these drinks. Both citric acid (E 330) and potassium sorbate (E 220) – long considered non-harmful – are now being probed for their cytotoxicity liability, especially when used in high doses over a long period. E 330 has been reported for its potential teratogenic effect and chronic consumption of E 220 at levels higher than maximum acceptable human E 220 level of 25 mg/kg body weight has been shown to be potentially both cytotoxic and genotoxic (79)(80). This development calls for re-evaluation by relevant supervisory authorities of the plethora of preservatives being used by our own local beverage manufacturers. Tartrazine is a synthetic lemon yellow azo dye primarily used as a food colouring with a maximum acceptable daily human limit of 7.5 mg/kg. Safety concerns over the use of tartrazine as a food colouring additive are mounting due to the reports of an association between it and increased risk of oxidative stress, cytotoxic and genotoxic effects in animal studies (81)(82)(83)(84)(85) and of developmental neurobehavioural maladjustment in children (86). Sunset yellow (FCF E 110) is a colouring agent which decades ago was considered not to pose any

significant health risks (87) is being re-evaluated for safety based on more recent reports of potential cytotoxicity and genotoxicity risks, especially when combined with one or more other food additives (88). Toxicity due to Sunset yellow has been reportedly aggravated when combined with tartrazine or with brilliant blue dye (88)(89). The increased association of morbidities cutting across the different systems – cardiovascular, endocrine, respiratory, musculoskeletal, etc. systems has attracted focus on the safety of artificial food flavouring chemicals just like other food additives. The increased health risks due to these food additives are viewed to be linked to the presence of chemicals i.e., linalool, ethyl vanillin, cinnamaldehyde, vanillin, ethyl maltol, menthol, and benzaldehyde (89) in them. Certain synthetic flavouring chemicals including some in the present study have been shown to induce reactive oxygen species generation, cytotoxicity, and genotoxicity. (90)(91)(92)(93). Synthetic orange food flavouring has been shown to be genotoxic to both plant and mice(94); melon flavourings shown to induce reactive oxygen species-linked cellular toxicity (93); artificial chocolate and vanilla shown to be cytotoxic, genotoxic, and mutagenic to mouse bone marrow cells; and artificial butter flavouring to have induced acute lethality in *Artemia salina* larvae and induced neurotoxicity and testicular in rodents (96)(97). These are toxicities associated with a few of the artificial flavouring chemicals encountered in this study. Thus, there is an urgent need to determine the safety of the catalogue of the flavorings i.e., brandy, butterscotch, ginger, coffee, caramel, Schnapp, gin, cream, and marula, chocolate being made use of by the local foods and drinks manufacturers. Finally, our findings indicate some of the brands have included/blended into them up to six different medicinal plant extracts – several of which their toxicity potential is unstated or unknown, up to 8 different food additives – with equally unproven safety, and in many instances, high alcohol content. This practice adds the potential health risks inherent in these chemicals in the consumer. Con-current use or consumption of two or more food additives has been shown to result in the exaggeration of their individual toxicities (97)(98). When the health risks from the food additives are combined with alcohol-related risks, on one hand, and with those arising from the inclusion of medicinal plant extracts in these drink brands, on the other hand, the long-term cumulative effects may result in the emergence of a myriad of chronic diseases such as asthma, dermatological disorders, cardiovascular diseases, childhood learning and attention deficit hyperactivity disorders, renal complications, migraine, obesity, cancer, and mood disorders (97)(98).

CONCLUSION AND RECOMMENDATIONS

Alcohol-related abuse and the potential health risks are on the increase in some Nigerian cities due to the availability of low-cost sachet/other low-volume alcoholic/non-alcoholic brands, and the practice of including some ‘tonic’ and ‘aphrodisiac’ medicinal extracts in them. To curb this tide and mitigate the attendant negative health impact, the relevant regulatory authorities need to step up their supervisory roles in the safety evaluation, registration, and production monitoring as well as post-marketing surveillance of these brands.

REFERENCES

- (1) Fishbain, D. A., Rosomoff, H. L., & Rosomoff, R. S. (1992). Drug abuse, dependence, and addiction in chronic pain patients. *The Clinical journal of pain*, 8(2), 77-85.
- (2) Osonuga, A. A., Ogunmoroti, B. D., Osonuga, A., & Da'costa, A. (2019). Alcohol use among secondary school students in Nigeria: A worrisome trend. *New Nigerian Journal of Clinical Research*, 8(14), 54.
- (3) Adamson, T. A., Ogunlesi, A. O., LufemiMorakinyo, O., Onifade, P. O., Erinosh, O., Adewuyi, A. A., Fasiku D. A., Adebowale, ogunwale A. & Somoye, E. B. (2015). Descriptive national survey of substance use in Nigeria. *Journal of Addiction Research & Therapy*, 6(3), 1-10.
- (4) Dumbili E. W. (2020). Drinking practices and alcohol-related problems among Nigerian students, *Drugs: Education, Prevention and Policy*, 27:3, 238-247.
- (5) Adeloye D., Olawole-Isaac A., Auta A., Dewan M. T., Omoyele C., Ezeigwe N., Jacobs W., Mpazanje R. G., Harhay M. O., Alemu W. & Adewole I. F. (2019). Epidemiology of harmful use of alcohol in Nigeria: a systematic review and meta-analysis. *Am J Drug Alcohol Abuse*.45(5):438-450.
- (6) Rukundo A. & Magambo J. (2013). Professional impotence: Impact of alcohol abuse on secondary schoolteachers in Uganda. *IJADR*, 2(2), 69 – 74.
- (7) Gossop, M., Marsden, J., Stewart, D., Lehmann, P., Edwards, C., Wilson, A., & Segar, G. (1998). Substance use, health and social problems of service users at 54 drug treatment agencies: Intake data from the National Treatment Outcome Research Study. *The British Journal of Psychiatry*, 173(2), 166-171.
- (8) Gossop, M., Marsden, J., Stewart, D., & Kidd, T. (2003). The national treatment outcome research study (NTORS): 4–5 year follow-up results. *Addiction*, 98(3), 291-303.
- (9) Lukaszewicz M., Falissard B., Michel L., Neveu X., Reynaud M. & Gasquet I. (2007). Prevalence and factors associated with alcohol and drug-related disorders in prison: a French national study. *Subst Abuse Treat Prev Policy*. 2:1. PMID: 17204156; PMCID: PMC1779267.
- (10) Athyros, V. G., Liberopoulos, E. N., Mikhailidis, D. P., Papageorgiou, A. A., Ganotakis, E. S., Tziomalos, K., ... & Elisaf, M. (2007). Association of drinking pattern and alcohol beverage type with the prevalence of metabolic syndrome, diabetes, coronary heart disease, stroke, and peripheral arterial disease in a Mediterranean cohort. *Angiology*, 58(6), 689-697.
- (11) Zhou, Y., Zheng, J., Li, S., Zhou, T., Zhang, P., & Li, H. B. (2016). Alcoholic beverage consumption and chronic diseases. *International journal of environmental research and public health*, 13(6), 522.
- (12) Mwele, J. K. (2009). *Perceived impact of packaging on alcohol consumption: a case of the University of Nairobi students* (Doctoral dissertation, University of Nairobi).
- (13) Hoel, E., Azalde, G., Munthali, A. C., Eide, A. H., Natvig, H., & Braathen, S. H. (2014). Context and consequences of liquor sachets use among young people in Malawi. *African Journal of Drug and Alcohol Studies*, 13(2), 97-106.
- (14) Smart, M., Mendoza, H., Mutebi, A., Milam, A. J., & Tumwesigye, N. M. (2021). Impact of the sachet alcohol ban on alcohol availability in Uganda. *Journal of Studies on Alcohol and Drugs*, 82(4), 511-515.
- (15) Potts, L. F., Luzzio, F. A., Smith, S. C., Hetman, M., Champy, P., & Litvan, I. (2012). Annonacin in *Asimina triloba* fruit: Implication for neurotoxicity. *Neurotoxicology*, 33(1), 53-58. (16) Levine, R. A., Richards, K. M., Tran, K., Luo, R., Thomas, A. L., & Smith, R. E. (2015). Determination of neurotoxic acetogenins in pawpaw (*Asimina triloba*) fruit by LC-HRMS. *Journal of agricultural and food chemistry*, 63(4), 1053-1056.
- (17) Ogunsina, O. I. (2020). Evaluation of antiplasmodial and immunomodulatory effect of methanolic stem bark extract of *Lannea acidia* (Doctoral dissertation, Ph. D Thesis).
- (18) Hamid K. M., Muhammad A. I., Balogun A. O., Nkom, D. M., Usman, A. B., & Aliyu, M. (2022). In-Vitro Cytotoxic and Proliferative Activity of Three Plant Extract on Human Peripheral Blood Mononuclear Cells (PBMCs). *Fountain Journal of Natural and Applied Sciences*, 11(2).
- (19) Han, H. J., Kim, H. Y., Choi, J. J., Ahn, S. Y., Lee, S. H., Oh, K. W., & Kim, S. Y. (2013). Effects of red ginseng extract on sleeping behaviors in human volunteers. *Journal of ethnopharmacology*, 149(2), 597-599.
- (20) Park, J. S., Kim, S. H., Han, K. M., Kim, Y. S., Kwon, E., Paek, S. H., ... & Kang, B. C. (2022). Efficacy and safety evaluation of black ginseng (*Panax ginseng* CA Mey.) extract (CJ EnerG): broad spectrum cytotoxic activity in human cancer cell lines and 28-day repeated oral toxicity study in Sprague-Dawley rats. *BMC complementary medicine and therapies*, 22(1), 1-13.
- (21) Koruk, S. T., Ozyilkan, E., Kaya, P., Colak, D., Donderici, O., & Cesaretli, Y. (2005). Juniper tar poisoning. *Clinical toxicology*, 43(1), 47-49.

- (22) Chan, K., Zhang, H. W., & Lin, Z. X. (2012). Treatments used in complementary and alternative medicine. In *Side Effects of Drugs Annual* (Vol. 34, pp. 769-783). Elsevier.
- (23) López, M. D., Jordán, M. J., & Pascual-Villalobos, M. J. (2008). Toxic compounds in essential oils of coriander, caraway and basil active against stored rice pests. *Journal of Stored Products Research*, 44(3), 273-278.
- (24) Isbrucker, R. A., & Burdock, G. A. (2006). Risk and safety assessment on the consumption of licorice root (*Glycyrrhiza* sp.), its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. *Regulatory Toxicology and Pharmacology*, 46(3), 167-192.
- (25) Omar, H. R., Komarova, I., El-Ghonemi, M., Fathy, A., Rashad, R., Abdelmalak, H. D., Yerramadha, M. R., Ali Y., Helal E&Camporesi, E. M. (2012). Licorice abuse: Time to send a warning message. *Therapeutic Advances in Endocrinology and Metabolism*, 3(4), 125-138.
- (26) Böcker, D., & Breithardt, G. (1991). Induction of arrhythmia by licorice abuse. *Zeitschrift für Kardiologie*, 80(6), 389-391.
- (27) Koga, K., Kawamura, M., Iwase, H., & Yoshikawa, N. (2013). Intestinal absorption and biliary elimination of glycyrrhizic acid diethyl ester in rats. *Drug Design, Development and Therapy*, 7, 1235-1243.
- (28) Shields, M., Niazi, U., Badal, S., Yee, T., Sutcliffe, M. J., & Delgoda, R. (2009). Inhibition of CYP1A1 by quassinoids found in *Picrasma excelsa*. *Planta medica*, 75(02), 137-141.
- (29) Awodele, O., Couliadiy, A. G. V., Afolayan, G. O., Agagu, S., Omoseyindemi, B., & Busia, K. (2019). Toxicological evaluation of *Picralima nitida* in rodents. *Journal of Ethnopharmacology*, 236, 205-219.
- (30) KouitcheuMabeku, L. B., Kouam, J., Paul, A., & Etoa, F. X. (2008). Phytochemical screening and toxicological profile of methanolic extract of *Picralima nitida* fruit-rind (Apocynaceae). *Toxicological & Environmental Chemistry*, 90(4), 815-828.
- (31) BGOBGO, M., Mama, K. O. N. E., KOFFI, A. E., WAPPO, F. E. E. R. K., & YAPO, P. A. E. (2021). Testicular toxicity of the ethanolic extract of the stems of *Massularia acuminata* (G. Don) Bullock ex Hoyl in rats. *Journal of Toxicology and Environmental Health Sciences*, 13(2), 60-66.
- (32) Yakubu, M. T., Ajidagba, K. K., Akanji, M. A., Oladiji, M. A., Ajiboye, T. O., Ibrahim, K. O., Oguntoye SO, SalawuMO, & Nafiu, M. O. (2012). Toxicopathological effects of saponins from *Massularia acuminata* stem in male Wistar rats. *Nigerian Journal of Natural Products and Medicine*, 16, 1-10.
- (33) Osman, A. G., Ali, Z., Fantoukh, O., Raman, V., Kamdem, R. S., & Khan, I. (2020). Glycosides of ursane-type triterpenoid, benzophenone, and iridoid from *Vangueria agrestis* (Fadogia agrestis) and their anti-infective activities. *Natural product research*, 34(5), 683-691.
- (34) Yakubu, M. T., Oladiji, A. T., & Akanji, M. A. (2009). Mode of cellular toxicity of aqueous extract of *Fadogia agrestis* (Schweinf. Ex Hiern) stem in male rat liver and kidney. *Human & experimental toxicology*, 28(8), 469-478.
- (35) Abraham, K., Wöhrlein, F., Lindtner, O., Heinemeyer, G., & Lampen, A. (2010). Toxicology and risk assessment of coumarin: focus on human data. *Molecular nutrition & food research*, 54(2), 228-239.
- (36) Vanderperren, B., Rizzo, M., Angenot, L., Haufroid, V., Jadoul, M., & Hantson, P. (2005). Acute liver failure with renal impairment related to the abuse of senna anthraquinone glycosides. *Annals of Pharmacotherapy*, 39(7-8), 1353-1357.
- (37) Wang, J. B., Ma, Y. G., Zhang, P., Jin, C., Sun, Y. Q., Xiao, X. H., ... & Zhou, C. P. (2009). Effect of processing on the chemical contents and hepatic and renal toxicity of rhubarb studied by canonical correlation analysis. *Yao xue xue bao = Acta pharmaceutica Sinica*, 44(8), 885-890.
- (38) Cheng, Y., Zhang, H., Qu, L., He, Y., Routledge, M. N., Gong, Y. Y., & Qiao, B. (2020). Identification of rhein as the metabolite responsible for toxicity of rhubarb anthraquinones. *Food chemistry*, 331, 127363.
- (39) Santa Maria, A., Lopez, A., Diaz, M. M., Munoz-Mingarro, D., & Pozuelo, J. M. (1998). Evaluation of the Toxicity of Guarana within Vitro Bioassays. *Ecotoxicology and environmental safety*, 39(3), 164-167.
- (40) Zeidán-Chuliá, F., Gelain, D. P., Kolling, E. A., Rybarczyk-Filho, J. L., Ambrosi, P., Resende Terra, S., Pires A. S., Da Rocha J. B., Antônio Behr G. & Fonseca Moreira, J. C. (2013). Major components of energy drinks (caffeine, taurine, and guarana) exert cytotoxic effects on human neuronal SH-SY5Y cells by decreasing reactive oxygen species production. *Oxidative medicine and cellular longevity*, 2013.
- (41) Pennay, A., Lubman, D. I., & Miller, P. (2011). Combining energy drinks and alcohol: A recipe for trouble?. *Australian family physician*, 40(3), 104-107.
- (42) Jenkins, A. P. (1997). Herbal energizers: speed by any other name. *Journal of Physical Education, Recreation & Dance*, 68(2), 39-45.
- (43) Moustakas, D., Mezzio, M., Rodriguez, B. R., Constable, M. A., Mulligan, M. E., & Voura, E. B. (2015). Guarana provides additional stimulation over caffeine alone in the planarian model. *PloS one*, 10(4), e0123310.
- (44) Ehigiator, B. E., & Adikwu, E. (2020). Toxicity study of ethanolic stem bark extract of *Xylopi aethiopic a* on fertility indices of male rats: An experimental study. *International Journal of Reproductive j*, 18(4), 265.
- (45) Woode, E., Alhassan, A., & Abaidoo, C. S. (2012). Effect of xylopic acid on sex hormones and spermatogenesis in male rats. 5 (3): 28-297.
- (46) Manfo, F. P. T., Nantia, E. A., & Kuete, V. (2014). Hepatotoxicity and hepatoprotective effects of African medicinal plants. *Toxicological Survey of African Medicinal Plants*, 323-355.
- (47) Abubakar, M., Lawal, A., & Usman, M. (2010). Hepatotoxicity studies of sub-chronic administration of aqueous stem bark of *Khaya senegalensis* in albino rats. *Bayero Journal of Pure and Applied Sciences*, 3(1).
- (48) Dikibo, E., Ehimigbai, J., Eloka, C. C. V., Ekoh, S. N., Ezeah, G. A. C., & Okoro, C. J. (2012). The effect of mondiawhitei on the histology of the brain of wistar rat. *International Journal of Herbs and Pharmacological Research*, 1(3), 62-67.
- (49) Patnam, R., Kadali, S. S., Koumaglo, K. H., & Roy, R. (2005). A chlorinated coumarin lignan from the African medicinal plant, *Mondia whitei*. *Phytochemistry*, 66(6), 683-686.
- (50) Björnstad, K., Helander, A., Hultén, P., & Beck, O. (2009). Bioanalytical investigation of asarone in connection with *Acorus calamus* oil intoxications. *Journal of analytical toxicology*, 33(9), 604-609.
- (51) Patel, D. N., Ho, H. K., Tan, L. L., Tan, M. M. B., Zhang, Q., Low, M. Y., ... & Koh, H. L. (2015). Hepatotoxic potential of asarones: in vitro evaluation of hepatotoxicity and quantitative determination in herbal products. *Frontiers in pharmacology*, 6, 25.
- (52) Abel, G., & Göggelmann, W. (1986). Genotoxic activity of β -asarone and commercial *calamus* drugs. *Mutation Research/Environmental Mutagenesis and Related Subjects*, 164(4), 287. 1;164(4):287.
- (53) Zou, X., Liu, S. L., Zhou, J. Y., Wu, J., Ling, B. F., & Wang, R. P. (2012). Beta-asarone induces LoVo colon cancer cell apoptosis by up-regulation of caspases through a mitochondrial pathway in vitro and in vivo. *Asian Pacific Journal of Cancer Prevention*, 13(10), 5291-5298.
- (54) Uebel, T., Hermes, L., Haupenthal, S., Müller, L., & Esselen, M. (2021). α -Asarone, β -asarone, and γ -asarone: Current status of toxicological evaluation. *Journal of Applied Toxicology*, 41(8), 1166-1179.
- (55) European-Commission. Opinion of the Scientific Committee on Food on the Presence of β -Asarone in Flavours and Other Food Ingredients with Flavouring Properties.
- (56) *Cellular & Molecular Immunology*, 19(7), 855-857.
- (57) Kwon, Y. H., Banskota, S., Wang, H., Rossi, L., Grondin, J. A., Syed, S. A., Yousefi Y., Schertzer J. D., Morrison, K. M., Wade, M. G. & Khan, W. I. (2022). Chronic exposure to synthetic food

- colorant Allura Red AC promotes susceptibility to experimental colitis via intestinal serotonin in mice. *Nature Communications*, 13(1), 7617.
- (58) Liu, C., Zhan, S., Tian, Z., Li, N., Li, T., Wu, D., ... & Zhuang, X. (2022). Food Additives Associated with Gut Microbiota Alterations in Inflammatory Bowel Disease: Friends or Enemies?. *Nutrients*, 14(15), 3049.
- (59) Piper, J. D., & Piper, P. W. (2017). Benzoate and sorbate salts: a systematic review of the potential hazards of these invaluable preservatives and the expanding spectrum of clinical uses for sodium benzoate. *Comprehensive reviews in food science and food safety*, 16(5), 868-880.
- (60) Zengin, N., Yüzbaşıoğlu, D., Ünal, F. A. T. M., Yılmaz, S., & Aksoy, H. (2011). The evaluation of the genotoxicity of two food preservatives: sodium benzoate and potassium benzoate. *Food and Chemical Toxicology*, 49(4), 763-769.
- (61) Rais, N., Ved, A., Shadab, M., Ahmad, R., & Shahid, M. (2023). Taurine, a non-proteinous essential amino acid for human body systems: an overview. *Arab Gulf Journal of Scientific Research*, 41(1), 48-66.
- (62) El-Batch, M., Hassan, A. M., & Mahmoud, H. A. (2011). Taurine is more effective than melatonin on cytochrome P450 2E1 and some oxidative stress markers in streptozotocin-induced diabetic rats. *Journal of Agricultural and Food Chemistry*, 59(9), 4995-5000. doi: 10.1021/jf1049547.
- (62) Shao, A., & Hathcock, J. N. (2008). Risk assessment for the amino acids taurine, L-glutamine and L-arginine. *Regulatory Toxicology and Pharmacology*, 50(3), 376-399. doi: 10.1016/j.yrtph.2008.01.004.
- (63) El-Batch, M., Hassan, A. M., & Mahmoud, H. A. (2011). Taurine is more effective than melatonin on cytochrome P450 2E1 and some oxidative stress markers in streptozotocin-induced diabetic rats. *Journal of Agricultural and Food Chemistry*, 59(9), 4995-5000.
- (64) Sholeye, O., Akinyemi, O., & Oyewole, B. (2022). Caffeinated beverage consumption among adolescents in Sagamu, Nigeria: implications for health promotion. *The Pan African Medical Journal*, 41.
- (65) Akpogheli, O. J., Igbuku, U. A., & Esemedafe, U. J. (2020). Evaluation and consequences of the pH and caffeine content of energy drinks marketed in Delta State, Nigeria. *Journal of Chemical Society of Nigeria*, 45(4).
- (66) Reissig, C. J., Strain, E. C., & Griffiths, R. R. (2009). Caffeinated energy drinks—a growing problem. *Drug and alcohol dependence*, 99(1-3), 1-10.
- (67) Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A., & Feeley, M. (2003). Effects of caffeine on human health. *Food Additives & Contaminants*, 20(1), 1-30.
- (68) Gunja, N., & Brown, J. A. (2012). Energy drinks: health risks and toxicity. *Medical Journal of Australia*, 196(1), 46-49.
- (69) Pennay, A., Lubman, D. I., & Miller, P. (2011). Combining energy drinks and alcohol: A recipe for trouble? *Australian family physician*, 40(3), 104-107.
- (70) Marczynski, C. A., & Fillmore, M. T. (2014). Energy drinks mixed with alcohol: what are the risks? *Nutrition reviews*, 72(suppl_1), 98-107.
- (71) Santa Maria, A., Lopez, A., Diaz, M. M., Munoz-Mingarro, D., & Pozuelo, J. M. (1998). Evaluation of the Toxicity of Guarana within *Vitro* Bioassays. *Ecotoxicology and environmental safety*, 39(3), 164-167.
- (72) Choudhary, A. K., & Pretorius, E. (2017). Revisiting the safety of aspartame. *Nutrition reviews*, 75(9), 718-730.
- (73) Olney, J. W., Farber, N. B., Spitznagel, E., & Robins, L. N. (1996). Increasing brain tumor rates: is there a link to aspartame? *Journal of Neuropathology & Experimental Neurology*, 55(11), 1115-1123.
- (74) Humphries, P., Pretorius, E., & Naude, H. (2008). Direct and indirect cellular effects of aspartame on the brain. *European journal of clinical nutrition*, 62(4), 451-462.
- (75) Lindseth, G. N., Coolahan, S. E., Petros, T. V., & Lindseth, P. D. (2014). Neurobehavioral effects of aspartame consumption. *Research in nursing & health*, 37(3), 185-193.
- (76) Bandyopadhyay, A., Ghoshal, S., & Mukherjee, A. (2008). Genotoxicity testing of low-calorie sweeteners: aspartame, acesulfame-K, and saccharin. *Drug and chemical toxicology*, 31(4), 447-457.
- (77) Wang, R., Li, Y., Mu, W., Li, Z., Sun, J., Wang, B., Zhong Z, Luo X, Xie C, & Huang, Y. (2018). Mulberry leaf extract reduces the glycemic indexes of four common dietary carbohydrates. *Medicine*, 97(34).
- (78) Maresch, C. C., Petry, S. F., Theis, S., Bösny-Westphal, A., & Linn, T. (2017). Low glycemic index prototype isomaltulose—update of clinical trials. *Nutrients*, 9(4), 381.
- (79) PEKMEZEKMEK, A. B., BİNOKAY, U. S., AKILLIOĞLU, K., & SERTDEMİR, Y. (2013). Evaluation of E330-induced developmental toxicity using FETAX. *Turkish Journal of Biology*, 37(3), 265-272.
- (80) Dehghan, P., Mohammadi, A., Mohammadzadeh-Aghdash, H., & Dolatabadi, J. E. N. (2018). Pharmacokinetic and toxicological aspects of potassium sorbate food additive and its constituents. *Trends in Food Science & Technology*, 80, 123-130.
- (81) Carocho, M., Barreiro, M. F., Morales, P., & Ferreira, I. C. (2014). Adding molecules to food, pros and cons: A review on synthetic and natural food additives. *Comprehensive reviews in food science and food safety*, 13(4), 377-399.
- (82) El-Desoky, G. E., Wabaidur, S. M., AlOthman, Z. A., & Habila, M. A. (2020). Regulatory role of nano-curcumin against tartrazine-induced oxidative stress, apoptosis-related genes expression, and genotoxicity in rats. *Molecules*, 25(24), 5801.
- (83) EFSA Panel on Food Additives and Nutrient Sources Added to Food. (2009). Scientific Opinion on the re-evaluation of Tartrazine (E 102). *EFSA Journal*, 7(11), 1331.
- (84) Sasaki, Y. F., Kawaguchi, S., Kamaya, A., Ohshita, M., Kabasawa, K., Iwama, K., Taniguchi K, & Tsuda, S. (2002). The comet assay with 8 mouse organs: results with 39 currently used food additives. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 519(1-2), 103-119.
- (85) Mehedi, N., Mokrane, N., Alami, O., Ainad-Tabet, S., Zaoui, C., Kheroua, O., & Saidi, D. (2013). A thirteen week ad libitum administration toxicity study of tartrazine in Swiss mice. *African journal of biotechnology*, 12(28).
- (86) Weiss, B. (2012). Synthetic food colors and neurobehavioral hazards: the view from environmental health research. *Environmental health perspectives*, 120(1), 1-5.
- (87) Gaunt, I. F., Mason, P. L., Grasso, P., & Kiss, I. S. (1974). Long-term toxicity of Sunset Yellow FCF in mice. *Food and cosmetics toxicology*, 12(1), 1-9.
- (88) Abd Elhalem, S., EL-Atrash, A., Osman, A., Sherif, A., & Salim, E. (2016). Short term toxicity of food additive azo dye, sunset yellow (E110), at low doses, in male Sprague-Dawley rats. *Egypt. J. Exp. Biol. Zool*, 12, 13-21.
- (88) Kaya, S. I., Cetinkaya, A., & Ozkan, S. A. (2021). Latest advances on the nanomaterials-based electrochemical analysis of azo toxic dyes Sunset Yellow and Tartrazine in food samples. *Food and Chemical Toxicology*, 156, 112524.
- (89) Koç, K., & Pandir, D. (2018). All aspect of toxic effect of brilliant blue and sunset yellow in *Allium cepa* roots. *Cytotechnology*, 70, 449-463.
- (90) Stefaniak, A. B., LeBouf, R. F., Ranpara, A. C., & Leonard, S. S. (2021). Toxicology of flavoring-and cannabis-containing e-liquids used in electronic delivery systems. *Pharmacology & therapeutics*, 224, 107838.
- (91) Moran, E. J., Easterday, O. D., & Boser, B. L. (1980). Acute oral toxicity of selected flavour chemicals. *Drug and Chemical Toxicology*, 3(3), 249-258.
- (92) Shibamoto, T. (2014). Diacetyl: occurrence, analysis, and toxicity. *Journal of agricultural and food chemistry*, 62(18), 4048-4053.
- (93) Yogeswaran, S., & Rahman, I. (2022). Differences in acellular reactive oxygen species (ROS) generation by E-cigarettes containing synthetic nicotine and tobacco-derived nicotine. *Toxics*, 10(3), 134.
- (94) Sousa Sales, I. M., Sousa Barbosa, J., Silva dos Santos, F. K., Cavalcanti Carneiro da Silva, F., Pinheiro Ferreira, P. M., de

- Castro e Sousa, J. M., & Peron, A. P. (2017). Assessment of grape, plum and orange synthetic food flavourings using in vivo acute toxicity tests. *Food Technology and Biotechnology*, 55(1), 131-137.
- (95) Sales, I. M. S., Silva, J. M., Moura, E. S. R., Alves, F. D. S., Silva, F. C. C., Sousa, J. M. C., & Peron, A. P. (2017). Toxicity of synthetic flavorings, nature identical and artificial, to hematopoietic tissue cells of rodents. *Brazilian Journal of Biology*, 78, 306-310.
- (96) Nunes, N. M. F., do Nascimento Silva, J., Conceicao, M. L. P., da Costa Junior, J. S., da Silva Sousa, E., das Dores Alves de OLIVEIRA, M., M., Maria das Graças Lopes CITÓ, A., Dittz, D., Peron, A.P. & Ferreira, P. M. P. (2023). In vitro and in vivo acute toxicity of an artificial butter flavoring. *Journal of Toxicology and Environmental Health, Part A*, 86(6), 181-197.
- (97) Bawazir, A. E. (2016). Evaluation of neurotoxicity and testicular toxicity of artificial Butter flavorings. *Int. J. Pharm. Res. Allied Sci*, 5(1), 248-258.
- (98) Fındıklı, Z., & Türkoğlu, Ş. (2014). Determination of the effects of some artificial sweeteners on human peripheral lymphocytes using the comet assay. *Journal of Toxicology and Environmental Health Sciences*, 6(8), 147-153.
- (99) Sambu, S., Hemaram, U., Murugan, R., & Alsofi, A. A. (2022). Toxicological and teratogenic effect of various food additives: an updated review. *BioMed Research International*, 2022(2): 1-11.
