"Alcohol use in mouthwash and possible oral health concerns"

Muhammad Wasif Haq,[1] Mehwish Batool,[2] Syed Hammad Ahsan,[3] Navid Rashid Qureshi[4]
4th Prof B.D.S Students,[1,2] Liaquat College of Medicine and Dentistry, Karachi.[3,4]

Abstract

Objective: To establish the presence and quantify Ethanol in commercially available mouthwashes.

Methods: Samples from twelve commercially available mouthwashes were tested for the presence of Ethanol followed by the estimation of percentage of Ethanol in five brands in Pakistan Council of Scientific and Industrial Research (P.C.S.I.R) and Husein Ebrahim Jamal (H.E.J.) labs, Karachi.

Results: Ten out of twelve brands of mouthwashes were found to be Ethanol positive.

Conclusion: Alcohol (Ethanol) in the mouthwashes does not contribute to any therapeutic action. It is alarming to find the presence of alcohol in the mouthwashes which claim to contain no alcohol (JPMA 59:186; 2009).

Introduction

Mouthwashes are considered beneficial in the prevention and treatment of variety of oral or orophryngeal diseases such as gingivitis, periodontitis and other inflammatory conditions. Apart from the various therapeutically active ingredients in the mouthwashes such as essential oils, Chlorhexidine, Fluoride, Potassium Nitrate and Benzydamine, one ingredient that is present generally in every mouthwash is "alcohol" (Ethanol, the term alcohol and Ethanol are used interchangeably in this article) that is in a concentration of 0-27% as compared to the alcohol content in beer (4%) and wine (12%). Ethanol by virtue of its structural configuration is bipolar that helps it dissolve hydrophobic as well as hydrophilic components.

The concentration of alcohol used in the mouthwash lags behind the optimum concentration of 50% to 70% at which alcohol is able to exert its antiseptic effect, hence except for its use as a solvent, alcohol in the mouthwash does not contribute to any other therapeutic effect. Due to this reason, alcohol free mouthwashes in the clinical trials

have proven to be as effective as alcohol based mouthwashes, with the former having lesser side effects.[1]

It has been postulated that alcohol in the mouthwash in reference to its local effects and metabolism, acts similarly to alcohol in the beverages.[2] As mouthwashes are kept in contact with oral mucosa, there is absorption of various ingredients including alcohol because of rich blood supply and relatively high permeability of oral mucosa. This has been measured by estimation of urinary excretion of Ethyl glucoronide (product of Ethanol metabolism) in concentration of as minimum as 50 ng/ml and as maximum as 300ng/ml after rinsing with 12% Ethanol based mouthwash.[3] Similarly alcohol has average oral fluid to blood concentration ratio of 1.07 when compared with few other drugs such as Barbiturates (0.3) and Diazepam (0.01-0.02).[4] The breath analyzers (used for detection of alcohol consumption) show positive readings after rinsing with alcohol based mouthwashes implicating that effect of alcohol in mouth is greater on rinsing than on swallowing.[5]

The metabolism of alcohol starts intra-orally by the normal oral flora that results in the production of well known toxic metabolite acetaldehyde.[6] Oral mucosa unlike most tissues of body, lacks alcohol dehydrogenase due to which acetaldehyde may be accumulated for a long duration of time in the mouth before being cleared.

Research has shown the permeability of oral mucosa to be directly proportional to the increase in concentration of Ethanol such that the mucosal permeability being greater at 15% Ethanol than at 5% Ethanol and sharply rises from 25% Ethanol to 50% Ethanol, beyond which no increase in the permeability was observed (Figure).[7] Such an increase in mucosal permeability has been evidenced to enhance the penetration of carcinogens such as Nitrosnornicotine.[8]

Considering the above mentioned scientific data that emphasizes on risks of high alcohol content in mouthwash, we planned a study to determine the qualitative and quantitative presence of Ethanol in commercially available mouthwashes in Pakistan; products labeling alcohol and those not labeling alcohol.

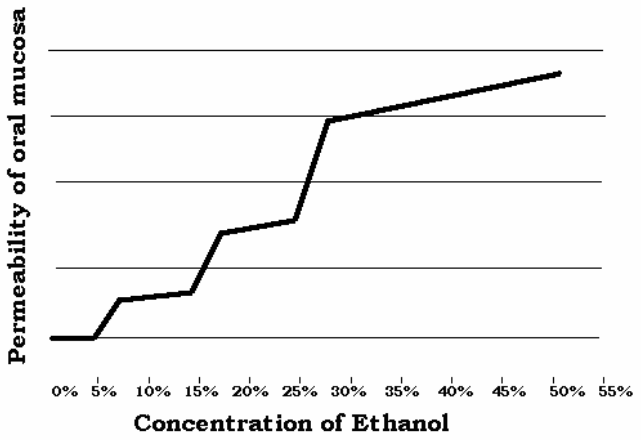

Figure: Increase in the permeability of oral mucosa in a stepwise pattern in relation to increasing concentrations of Ethanol. Ethanol concentrations above 50% cause no change in the permeability of oral mucosa.

Material and Methods

Four samples each from twelve commercially available mouthwashes were collected from three super stores in Karachi. The batch number, manufacturing date and expiry date of the samples were noted.

A total of four tests were performed. The tests were divided into the qualitative tests used for the detection of alcohol in the samples and the quantitative tests.

The qualitative/preliminary tests employed three tests namely Iodoform test, Chromic Acid test and Nuclear Magnetic Resonance (N.M.R.) spectroscopy.

In the Iodoform test , a standard volume of 5 ml of the sample was taken and reacted with 2 ml of Iodine and 5% NaOH. Samples of twelve brands of mouthwashes were tested using this reaction. The presence of Ethanol is indicated by the formation of yellow precipitates of Iodoform (Triiodomethane).[9]

The second test employed was Chromic Acid test in which Potassium Dichromate oxidizes alcohol that was indicated by the color change of Potassium Dichromate from orange to green, this is the same reaction used in the Breath Analyzers to measure concentration of alcohol. A standard volume of 3 ml of every sample was taken and reacted with few drops of concentrated Sulfuric acid. Twelve samples were tested using this reaction.

After the two qualitative tests, two alcohol negative samples were excluded while from remaining ten samples; five mouthwashes were selected randomly (non-probability sampling) for further confirmatory tests for the presence of Ethanol followed by estimation of percentage of Ethanol in the selected five samples.

In the third qualitative test, N.M.R. spectroscopy was utilized. This technique detects radio frequency absorbed by protons at applied magnetic fields denoting chemical shifts on the recording paper. 3 ml of the sample was taken. Five samples were submitted for this test.

In the fourth test, quantitative assessment of Ethanol by Gas Chromatography (G.C.) was performed. To rule out the element of bias and variability, two samples were submitted in the lab of P.C.S.I.R and three samples were submitted in H.E.J. labs.

Results

In the preliminary tests Iodoform and Chromic acid test, twelve samples of mouthwashes namely Listerine, Enziclor, Signal, Prodent, Niflam, Protect (Alcohol free),

Oral B (Alcohol free), Clinica, Neo-nexus, Hi-Paradent, Pepsodent (Alcohol free) and Enliven (Alcohol free) were tested. Except for two products; Oral B (Alcohol free) and Enliven (Alcohol free), all the ten remaining samples gave positive Ethanol reaction (Table-1). The samples that did not contain alcohol were not subjected for further confirmatory tests. In N.M.R. test, five samples namely Listerine, Enziclor, Signal, Protect (Alcohol free) and Pepsodent (Alcohol free) were selected and confirmed to be Ethanol positive .In the quantitative assessment of Ethanol in mouthwashes by G.C., the percentage of Ethanol was determined in the selected five samples that were confirmed to contain Ethanol by N.M.R., the percentage of alcohol observed in these samples by P.C.S.I.R. and H.E.J. labs is listed in Table 2.

Table 1: Presence of Ethanol in samples by Iodoform, Chromic Acid and N.M.R test.

Brand Name of Mouthwash	Ethanol Iodoform/Chronic Acid/NMR
1.Listerine*	Positive
2.Enziclor*	Positive
3.Signal*	Positive
4.Prodent	Positive
5.Niflam	Positive
6.Protect (Alcohol free)*	Positive
7.Oral B (Alcohol free)	Negative
8.Clinica	Positive
9.Neo-nexus	Positive
10.Hi-Paradent	Positive
11.Pepsodent (Alcohol free)*	Positive
12.Enliven (Alcohol free)	Negative

The marked (*) samples were tested by N.M.R. also and found to be Ethanol positive.

Table 2: Results of percentage of Ethanol determined by G.C.

Brand Name of mouthwash	Percentage of Ethanol
1.Listerine	24.5%
2.Protect (Alcohol free)	3.5%
3.Signal	13.8%
4.Enziclor	3.58%
5.Pepsodent (Alcohol free)	2.89%

The samples 1 and 2 were tested in P.C.S.I.R. labs while 3,4 and 5 in H.E.J. labs.

Discussion

It is a matter of serious concern that alcohol is present in many mouthwashes labeled as without alcohol and in brands that do not mention any information regarding presence of alcohol on the display panel of their products. Such products are being sold over the counter without the consumer knowing about it. The Drug Act, 1976 states that in Pakistan companies require to mention their active ingredients. Since alcohol is not an active ingredient therapeutically, many companies defer from listing alcohol in their list of ingredients.[10] Only few brands such as Listerine, Macleans, Colgate, Smokers and Signals are currently mentioning alcohol in the ingredients with even fewer brands mentioning the percentage of alcohol in the product.

Although not therapeutically active, Ethanol in the mouthwash has been proven to produce multiple other effects many of which are not beneficial and un-necessary for the user. These range from a characteristic burning sensation upon contact with the oral mucosa by activation of vanilloid receptor-1; a heat gated ion channel to a dehydrating effect on the oral mucosa.[11,12] Due to the astringent action of ethanol, the use of high alcohol mouthwashes in patients with radiation mucositis is not recommended.[13] Patients with Sjögren's syndrome should avoid alcohol based mouthwash as it may aggravate xerostomia, and with decreased salivary flow locally, atrophic changes of oral epithelium may occur. Similarly people on Alcohol Withdrawal therapy or patients on Disulfiram therapy should also avoid using such formulations. American Dental Association (ADA) advices patients of burning mouth syndrome to avoid irritating substances such as mouthwashes.[14] Similarly alcohol is a known cause of halitosis and mouthwashes only temporarily relief the problem.[15]

Alcohol is an irritant to epithelium and in animal studies; the topically applied alcohol was linked with increased occurrence of tumours.[16] Inflammatory changes may also develop that may induce hyperkeratosis and atrophy of mucosa. In a study that involved 40 hamsters, two hamsters showed areas of hyper-parakeratinazation, loss of cellular cohesion in basal cell layers with mononuclear inflammatory cells when treated with 23% Alcohol based mouthwash.[17]

Studies and case reports link such a high percentage of alcohol in certain mouthwashes with development of leukoplakia, the lesion was reversible when the mouthwash was stopped.[18] There has also been concern about the correlation of high level of alcohol in the mouthwash with increased susceptibility towards oral cancer.[19] Although to date, no scientific data establishes it as an etiological factor but few cases have been documented in literature in which alcohol containing mouthwashes are suspected, especially of a patient who suffered from multiple recurrent oral cancers, the patient gave a long history of using 14% alcohol based mouthwash.[18] However, it must be stated that other local and systemic factors can aggravate the susceptibility towards oral cancer.

The production of acetaldehyde intra-orally is also a matter of grave concern. Acetaldehyde is a known carcinogen and has been shown to cause hyperplastic and

hyperproliferative changes in epithelium as well as it binds to D.N.A. and proteins and destroys folate.[20] This may lead to decreased folic acid resulting in keratinzation abnormalities leading to atrophy. Alcohol acts against hepatic neo-antigens due to which tumour proliferation may go unchecked and it also influences stem cell in the basal cell layer by intracellular and intercellular pathway, a step suggested to be of importance in development of oral cancer.[21]

Stromyelysin 3; a gene involved in cancer metastasis has been shown to be activated by acetaldehyde.[22] In an vitro study, acetaldehyde production from mouthwash was proven to be cytotoxic for gingival fibroblasts.[23] With regards to cancer susceptibility from alcohol, Asian population is more susceptible because of genetic polymorphisms in Alcohol Dehydrogenase (ADH) genotype that contributes to slower metabolism and prolonged effects of ethanol metabolites.[24]

In relation to alcohol effect on composite restorations, mouthwashes having high level of alcohol have been studied to affect color and hardness of composite restorations.[25]

FDA recommendations:

With raising concerns over safety of high alcohol based mouthwashes, the Food and Drug Administration (FDA) recommended following alcohol concentrations to be used according to different age levels (Table 3).[26]

Table 3: Percentage of Alcohol for oral drug products recommended by FDA.

Age limit	% of Alcohol
1.Chilren under 6 Years	Alcohol free, Otherwise 0.5% or less
2.Children between 6 to 12 Years	5% Alcohol
3.People over 12 Years	Not more than 10% Alcohol

Currently most Chlorhexidine mouthwashes in United States are formulated with maximum of 12% alcohol while few others are entirely alcohol free. The U.S. Consumer Product Safety Commission (CPSC) has proposed child resistant packaging for mouthwashes having 3 grams or more Ethanol because of over eighteen thousand cases of accidental ingestion by children over a period of nine years resulting in coma, seizures and hypoglycemia and two deaths reported so far.[27,28] In case of hypoglycemia; secondary to mouthwash ingestion, I/V glucose should be given. Although FDA does not establish a causal relation between alcohol in mouthwash and oral cancer, it suggests further research to be carried out in this area. Furthermore, American Cancer Society, National Cancer Institute (United States) and Cancer Research Center UK discourage the use of high alcohol based mouthwashes and categorize it as possible risk factor.

Conclusion

In the present study, alcohol was present in all the mouthwashes except for two products that were tested in this study. It is a matter of serious concern to find the presence of alcohol in the brands that claim to contain no amount of alcohol, hence it is suggested that the regulatory authorities of Pakistan and Pakistan Dental Association (P.D.A.) in particular should play an active role and address this issue. It is also recommended that the levels of alcohol in the mouthwash need to be monitored and only the limit necessary to dissolve active ingredients should be permitted as well as making sure that all the brands should be obliged to mention the exact percentage of alcohol as suggested by F.D.A. thereby helping the consumer to choose any brand depending upon the preferences. There is need for development of child resistant packaging for mouthwashes having high level of alcohol with instruction to keep out of reach of children clearly written on the display panel to avoid any accidental ingestion. We recommend that depending on the different ingredients and their role in the mouthwashes, these should be only prescribed when a patient requires it in certain conditions. With regards to susceptibility to increased risk towards oral cancer from high alcohol based mouthwashes, definitive and conclusive data is lacking and certainly there is a need for further studies to be carried out to have a clear picture of any association if at all from mouthwashes.

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