

Review Article

Mouthwashes and Their Use in Different Oral Conditions

Amit Parashar

Department of Periodontics, KLE VK Institute of Dental Sciences, Belgaum, Karnataka, India.

***Corresponding author**

Dr Amit Parashar , MDS,FAGE,FPFA

Email: captamitparashar@gmail.com

Abstract: Mouthwashes are medicated solutions used for gargling and rinsing the mouth. Many oral conditions require the use of a mouthwash, which can vary from oral malodour to periodontal disease to treatment of secondary infections like oral mucositis. A mouthwash may be recommended as an antimicrobial, a topical anti-inflammatory agent, a topical analgesic or for caries prevention. Many different mouthwashes are available now a day. Selection of an appropriate mouthwash depends on patient's oral condition, disease risk and efficiency and safety of mouthwash. The main objective of this review is to help the oral health care professionals to make the correct selection of mouthwash while dealing with different conditions of oral cavity.

Keywords: Mouthwash, Oral condition.

INTRODUCTION

Dental plaque is the main etiologic agent in the development and progression of gingival and periodontal diseases[1]. Principal means of preventing the development and progression of various periodontal diseases is mainly through mechanical removal of plaque through regular tooth brushing[2]. But for mentally or physically-handicapped patients who are unable to brush their teeth themselves or other individuals who lack the dexterity, skill or motivation for mechanical plaque removal, mouthwashes may aid in controlling dental plaque and periodontal disease[3]. Mouthwashes should never be used as sole means of oral hygiene but it should always be used in conjunction with mechanical plaque control measures.

The use of mouthwash to control plaque bacteria date back around 5000 years when the Chinese recommended the use of child's urine for the control of gingivitis[4]. Mouthwashes can be used for various preventative and therapeutic purposes viz. to treat oral infections, reduce inflammation, decrease halitosis and to deliver fluoride locally for preventing caries. The use of mouthwash is usually based on anecdotal evidence rather than scientific evidence especially for over-the-counter (OTC) products. This may often leads to the use of an inappropriate product and incorrect mode of application, leading to a failed treatment outcome[5]. The patient's ability to perform good mechanical oral hygiene practices, dental status, gingiva and oral mucosa, other oral diseases (xerostomia), and the efficacy of a mouthwash and its potential adverse

effects should be taken into consideration before recommending a particular mouthwash.

CHLORHEXIDINE

Chlorhexidine is a symmetrical bisbiguanide synthetic antiseptic consisting of four chlorophenyl rings and two biguanide groups connected by a hexamethylene bridge. The dicationic nature of Chlorhexidine makes it extremely interactive with anions, which is relevant to its efficacy, safety and side effects. It is available in three forms, digluconate, acetate and hydrochloride salts.

Chlorhexidine has broad spectrum antimicrobial activity. It is effective against both Gram-positive and Gram-negative bacteria including aerobes and anaerobes, yeasts, fungi and lipid enveloped viruses[6-7]. It increases the permeability of cell membrane followed by coagulation of cellular macromolecules[8]. It has also shown to reduce the adherence of *Porphyromonas gingivalis* to epithelial cells[9]. It does not interact with any microbial enzymes or receptors and hence does not lead to resistance from organisms[10].

Substantivity

The ability of drugs to adsorb onto or bind to soft and hard tissues is known as Substantivity[11-13]. It ensures that the effect is sustained for a longer period than just the time it is held in the mouth and thus it is suitable for plaque inhibition[12, 14]. Substantivity is influenced by concentration, pH, temperature and time for which the solution is held in mouth[13].

Safety

Chlorhexidine is poorly absorbed in the gastrointestinal tract and undergoes minimal metabolic cleavage in the body. Therefore, it shows very low toxicity. Its oral LD₅₀ is 1800mg/kg and i.v. LD₅₀ is 22mg/kg. Animal studies have revealed that primary route of Chlorhexidine excretion is through faeces. There is no evidence of carcinogenic substance formation and no teratogenic alterations have been reported on its long term use[15,16].

Clinical usage

Various preparations of Chlorhexidine mouthwashes are available across the globe. The Chlorhexidine mouthwash containing 0.2% Chlorhexidine should be used 10ml volume per rinse delivers 20mg of total dose of Chlorhexidine and those preparations containing 0.12% Chlorhexidine to be used 15ml volume per rinse delivers 18mg Chlorhexidine[17]. Segreto et al stated that the effect of Chlorhexidine is dose dependent not just depending on its concentration[18]. So, both of these formulations are effective. But the lower concentration of Chlorhexidine minimizes its side effects while maintaining its benefits. To ensure good compliance and efficacy, the accepted length of time for rinsing is 30 seconds[19]. Patients should be advised to rinse just before going to bed and after breakfast, with at least 30 minutes interval after tooth brushing.

Side effects: Flotra et al reported various local side effects of Chlorhexidine mouthwash[20]. These local side effects are:

1. Brown discoloration of the teeth, restorative materials and the tongue.
2. Alter taste sensation especially for salt taste.
3. Mucosal erosion with use of high concentration of Chlorhexidine rinse.
4. Parotid swelling in rare cases.
5. Increased rate of supragingival calculus formation.

Staining: Various mechanisms for Chlorhexidine staining were proposed[21-23]. They are:

1. Degradation of the Chlorhexidine to release parachloraniline.
2. Non-enzymatic browning reactions (Maillard reactions).
3. Protein denaturation by Chlorhexidine with metal sulphide formation.
4. Precipitation of anionic dietary chromogens by cationic antiseptics.

BENZYDAMINE HYDROCHLORIDE

Benzylamine hydrochloride is known for its analgesic, anaesthetic, anti-inflammatory and antimicrobial properties. The exact mechanism of action is not fully understood but it probably affects the prostaglandin and thromboxane production and decrease pro-inflammatory cytokine production.

Epstein et al. demonstrated that Benzylamine significantly reduces the duration, incidence and severity of radiation-induced mucositis[24]. Therefore, it is recommended for radiation-induced mucositis and ulcerative lesions like recurrent aphthous stomatitis.

ESSENTIAL OILS

Mouthwashes based on essential oils contain thymol, eucalyptol and menthol in an alcohol solvent. They are broad spectrum antimicrobial agents which decrease bacterial multiplication, aggregation and pathogenicity[25]. They act by destruction of bacterial cell and inhibition of bacterial enzymes. They also have anti-inflammatory activity, prostaglandin inhibitory activity and antioxidants activity. Sharma et al. stated that mouthwashes containing essential oils are effective in reducing oral malodour and gingivitis[26].

They can be recommended as an adjunct to mechanical plaque control measures especially in patients with gingival inflammation even with regular tooth brushing and flossing. They are contraindicated in children because of risk of ingestion and in patients suffering from dry mouth and oral mucosal disease because of ethanol based irritation and dryness.

CETYLPIRIDINIUM CHLORIDE AND SODIUM BENZOATE

Cetylpyridinium chloride is a quaternary ammonium compound with moderate plaque inhibitory activity[27,28]. It acts by binding to bacterial cell membrane because of its cationic nature thus causing disruption of cell membrane and leakage of intracellular components. The reason behind their moderate plaque inhibitory activity as compare to Chlorhexidine may be their rapid desorption from the oral mucosa and may also be related to their mono-cationic nature[12, 29, 30]. The single cationic group binds to mucosa providing mucosal retention but leaving few unattached sites for its antibacterial action.

Sodium benzoate disperses carbohydrate, fat, protein thereby weakens plaque attachment which can then be easily removed by toothbrushing.

TRICLOSAN

Triclosan (2, 4, 4'-trichloro-2'-hydroxydiphenyl ether) is a non-ionic antiseptic compound shows anti-inflammatory property and has been used in many toothpastes and mouthwashes[31]. Various studies have shown that Triclosan reduces the inflammatory reaction on the gingiva by sodium lauryl sulphate and reduce the severity and healing period of recurrent aphthous ulcers[32,33]. Gaffar et al stated Triclosan reduces the levels of inflammatory mediators (prostaglandins and leukotrienes) by inhibiting both cyclo-oxygenase and lipoxygenase pathways[34]. Triclosan also increases the binding ability of mouthwashes to the oral mucosa and thus being available for a longer period of time.

OXYGENATING AGENTS

Oxygenating agents such as Hydrogen peroxide, Sodium peroxyborate and peroxy carbonate act by liberating nascent oxygen to loosen debris, remove stains and kill anaerobic micro-organisms. They are bleaching agent having strong oxidising properties. They are also broad spectrum antimicrobial agents[35]. Oxygenating agents containing mouthwashes are recommended for acute ulcerative conditions, to relieve soreness caused by dentures, orthodontic appliances and for stain removal[36].

POVIDONE-IODINE CONTAINING MOUTHWASHES

Povidone-iodine is a broad spectrum antimicrobial having its affinity against bacteria, virus, fungi and protozoa. It is an iodophore in which iodine is loosely bound to Povidone thereby delivering free iodine to bacterial cell membrane. It reduces plaque formation and decreases the severity of gingivitis and radiation mucositis. It is contraindicated in individuals having sensitivity to iodine and pre-existing thyroid disorders[37].

ANTIBACTERIAL PEROXIDASE MOUTHWASHES

They contain enzymes like lysozyme, lactoferrin, lactoperoxidase and glucose oxidase which act against bacterial peroxidase. They restore antimicrobial activity of saliva hence, useful in cases of dry mouth, gingival inflammation and oral malodour[38]. Its long term use might pose a risk of dental erosion because of its low pH.

FLUORIDE CONTAINING MOUTHWASHES

These mouthwashes contain fluoride in various forms as either sodium fluoride (NaF) or acidulated phosphate fluoride (APF). They promote remineralisation of enamel with fluorapatite and fluor-hydroxyapatite, making enamel resistant to acid attack. Hence, they are useful in patients with high risk of dental caries, patients having xerostomia after undergoing radiation therapy and those undergoing orthodontic therapy[39]. They are contra-indicated in children less than six years of age because of risk of fluoride ingestion.

SODIUM BICARBONATE

It increases the salivary pH and suppresses the growth of aciduric bacteria. Therefore, it is recommended in patients with xerostomia and erosion.

ALCOHOL CONTENT OF MOUTHWASHES

Ethanol is used as a preservative and solvent in a concentration range of 5 – 27 % in various commercially available mouthwashes. It has antimicrobial activity against various bacteria, fungi

and viruses by causing protein denaturation and dissolution of lipids. Various studies have been done to determine the relationship between use of alcohol containing mouthwashes and the risk of developing oro-pharyngeal cancer.

McCulloch and Farah stated that there may be a direct association between the alcohol content of mouthwashes and the risk of development of oral cancer[40]. The risk of developing oro-pharyngeal cancer is nine times in smokers, five times in those who also drink alcohol, and five times in those who neither smoke nor drink alcohol. While Cole et al) demonstrated no relationship between the use of alcohol containing mouthwashes and the risk of development of oro-pharyngeal cancer[41]. Lachenmeier et al demonstrated acetaldehyde which is a toxic metabolite of ethanol, is formed from alcohol containing mouthwashes and their concentration in saliva is similar to those found after alcohol consumption[42].

Mouthwashes containing significant amount of alcohol have number of disadvantages also. Firstly, they are not accidentally swallowed by young children[43-44]. Secondly, the use of alcohol containing mouthwashes may increase the alcohol content of exhaled air and could change the readings of the police breath test[45]. Thirdly, alcohol containing mouthwashes have also shown to reduce the hardness of composite and hybrid resin restorations and may also alter the colour of composite restorations[46-47]. The use of alcohol containing mouthwashes should be restricted to short term under supervision until long term studies are available. The use of alcohol containing mouthwashes should be discouraged for long term use.

CLINICAL IMPLICATIONS

Mouthwashes can be used in various clinical conditions.

They can be used as an *adjunct* to mechanical oral hygiene procedure in conditions like:

- After subgingival scaling or root planing
- In patients having inadequate oral hygiene
- Post-scaling cervical hypersensitivity

They can be used to *replace* normal toothbrushing which is not possible in various conditions like:

- After periodontal surgical procedures
- After intermaxillary fixation
- During acute oral or gingival infection
- For mentally or physically handicapped patients

Mouthwashes for Different Oral Conditions (Table 1)

Table 1: Mouthwashes In Different Clinical Conditions [19].

Clinical Conditions	Treatment	Active Ingredients
Oral mucositis / oral sores (alcohol free)	Covering agent	Polyvinylpyrrolidone
	Anti-inflammatory	Benzydamine hydrochloride
	Antimicrobial	Chlorhexidine 0.12% Generic CHX 0.2% Povidone Iodine
	Analgesic / Anti-inflammatory / Antimicrobial	Benzydamine hydrochloride / Chlorhexidine
	Antimicrobial / Analgesic	Benzocaine / Chlorhexidine
Halitosis	Antimicrobial without flavouring	Generic CHX 0.2% Chlorhexidine 0.12% Chlorhexidine 0.2%
	Antimicrobial with flavouring	Chlorhexidine 0.2% Cetylpyridinium chloride, Triclosan with oil Essential oils
Xerostomia	Saliva substitute with antimicrobial properties	Betaine / Olive oil / Xylitol / Fluoride Various enzymes Cetylpyridinium chloride, Triclosan with oil
	Tooth protection - Fluoride	Sodium fluoride 0.05%
Periodontal (gum) diseases	Antimicrobial with / without flavouring	Chlorhexidine 0.2% Chlorhexidine 0.12% Benzydamine hydrochloride

Oral mucositis:

Oral mucositis is a complication which can be seen in patients after head and neck radiation therapy, chemotherapy and in bone marrow transplant cases[48-50]. Although the mechanism for development of oral mucositis is much complex, but it may occur from direct effect of cytotoxic drugs on oral epithelial cells in cancer patients[51]. Maintenance of oral hygiene and plaque control measures are important factors in the management of oral mucositis[50]. 0.12% or 0.2% Chlorhexidine mouthwashes can be used for this purpose but combination mouthwashes containing anti-inflammatory, analgesic, antimicrobial properties and covering agents are much more useful.

Halitosis:

Breath malodour is a common complaint among the general population which has a significant socioeconomic impact. Scully and Greenman stated that in 85% of cases, an oral cause can be found while extraoral causes (ENT pathologies, systemic diseases, metabolic or hormonal changes, hepatic or renal insufficiency, pulmonary diseases and GIT pathologies) can be found in rest 15% of the cases[52]. Intraoral causes mainly include tongue and tongue coating, periodontal diseases, deep carious lesions and dry mouth. A proper diagnosis is therefore essential and the treatment of oral malodour should preferably be cause related. Use of mouthwashes is a common practice in patients with oral malodour. The active ingredients in these mouthwashes are usually antimicrobial compounds like Chlorhexidine, Cetylpyridinium chloride, chlorine dioxide, hydrogen peroxide, essential oils and Triclosan[53].

Xerostomia

Xerostomia / Dry mouth is not a disease but a sign of an underlying disease or side effect of medications and radiation therapy for head and neck cancer treatment. Various changes occur in saliva after head and neck radiation therapy like decreased salivary flow, reduced pH and thick and pasty saliva hence, excellent plaque control and oral hygiene measures are essential[54-55]. Xerostomia is also a common sign in older age individuals. Various symptomatic treatment measures are available like salivary stimulation, avoidance of dry sticky food, saliva replacement therapy and maintenance of good oral hygiene[55]. Various preparations of mouthwashes containing Chlorhexidine, Cetylpyridinium chloride, Triclosan, fluoride in non alcohol base preparations are helpful[50,55].

Periodontal diseases

Gingival and Periodontal diseases are one of the most common diseases in the world[56,57]. Mechanical plaque control measures (toothbrushing and flossing) are of utmost importance in prevention of periodontal diseases. Chemical plaque control measures like use of mouthwash preparations containing 0.12% or 0.2% Chlorhexidine, Benzydamine chloride may also aid in prevention of periodontal diseases[58].

CONCLUSION

Mouthwashes can be used for various conditions, depending on the lesions present in the oral cavity. So, the oral health practitioners should be aware of various etiologic factors and predisposing conditions affecting a particular oral lesion. The use of mouthwash should be limited to a smaller period of time depending on the

lesion present and should always be used as an adjunct to mechanical plaque control measures (tooth brushing and flossing). Long term use of alcohol based mouthwashes should be discouraged.

REFERENCES

1. Adams D, Addy M; Mouthrinses. *Adv Dent Res.*, 1994; 8: 291-301.
2. Daly CG; Prescribing good oral hygiene for adults. *Aust Prescr*, 2009; 32: 72-5.
3. Dona BL, Grundemann LJ, Steinfort J, Timmerman MF; van der Weijden GA; The inhibitory effect of combining chlorhexidine and hydrogen peroxide on 3-day plaque accumulation. *J Clin Periodontol*, 1998; 25: 879-83.
4. Mandel ID; Chemotherapeutic agents for controlling plaque and gingivitis. *J Clin Periodontol*, 1988; 15: 488-98.
5. Lang NP, Tan WC, Krahenmann MA, Zwahlen MA; systematic review of the effects of full-mouth debridement with and without antiseptics in patients with chronic periodontitis. *J Clin Periodontol*, 2008; 35: 8-21.
6. Harbison MA, Hammer SM; Inactivation of human immunodeficiency virus by Betadine products and chlorhexidine. *J Acquir Immune Defic Syndr*, 1989; 2: 16-20.
7. Suci PA, Tyler BJ; Action of chlorhexidine digluconate against yeast and filamentous forms in an early-stage *Candida albicans* biofilm. *Antimicrob Agents Chemother*, 2002; 46: 3522-31.
8. Hennessy T; Antibacterial properties of Hibitane. *J Clin Periodontol*, 1977; 4: 36-48.
9. Grenier D; Effect of chlorhexidine on the adherence properties of *Porphyromonas gingivalis*. *J Clin Periodontol*, 1996; 23: 140-2.
10. Moran JM; Home-use oral hygiene products: mouthrinses. *Periodontol*, 2008; 48: 42-53.
11. Röllä G, Löe H, Schiöt C; Retention of chlorhexidine in the human oral cavity. *Arch Oral Biol*, 1971; 16: 1109-16.
12. Bonesvoll P, Lökken P, Röllä G; Influence of concentration, time, temperature and pH on the retention of chlorhexidine in the human oral cavity after mouth rinses. *Arch Oral Biol*, 1974; 19: 1025-9.
13. Bonesvoll P, Gjermo PA; comparison between chlorhexidine and some quaternary ammonium compounds with regard to retention, salivary concentration and plaque inhibitory effect in the human mouth after mouthrinses. *Arch Oral Biol*, 1978; 23: 289-94.
14. Gjermo P, Bonesvoll P, Röllä G; Relationship between plaque inhibiting effect and the retention of chlorhexidine in the oral cavity. *Arch Oral Biol*, 1974; 19: 1031-4.
15. Winrow M; Metabolic studies with radiolabelled chlorhexidine in animals and man. *J Periodont Res.*, 1973; 12 (suppl.): 45-8.
16. Faulkes E; Some toxicological observations of chlorhexidine. *J Periodont Res.*, 1973; 12 (suppl.): 131-48.
17. Binney A, Addy M, McKeown S, Everatt L; The effect of a commercially available triclosan-containing toothpaste compared to a sodium-fluoride-containing toothpaste and a chlorhexidine rinse on 4-day plaque regrowth. *J Clin Periodontol*, 1995; 22: 830-4.
18. Segreto VA, Collins EM, Beiswanger BB, Rosa M, Isaacs RL, Lang NP; A comparison of mouthrinses containing two concentrations of chlorhexidine. *Journal of Periodontal Research*, 1986; 21: 23-32.
19. Van der Weijden GA, Timmerman MF, Novotny AG, Rosema NA, Verkerk AA; Three different rinsing times and inhibition of plaque accumulation with chlorhexidine. *J Clin Periodontol*, 2005; 32: 89-92.
20. Flotra L, Gjermo P, Rolla G, Waerhaug J; Side effects of chlorhexidine mouthwashes. *Scandinavian Journal of Dental Research*, 1971; 79: 119-25.
21. Eriksen HM, Nordbo H, Kantanen H, Ellingsen JE; Chemical plaque control and extrinsic tooth discoloration. A review of possible mechanisms. *Journal of Clinical Periodontology*, 1985; 12: 345-50.
22. Addy M, Moran JM; Mechanisms of stain formation on teeth, in particular associated with metal ions and antiseptics. *Advances in Dental Research*, 1995; 9: 450-6.
23. Watts A, Addy M; Tooth discoloration and staining: A review of the literature. *British Dental Journal*, 2001; 190: 309-16.
24. Epstein JB, Silverman SJr, Paggiarino DA, Crockett S, Schubert MM, Senzer NN; Benzylamine HCl for prophylaxis of radiation-induced oral mucositis: results from a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Cancer*, 2001; 92: 875-85.
25. Fine DH, Furgang D, Sinatra K, Charles C, McGuire A, Kumar LD; In vivo antimicrobial effectiveness of an essential oil-containing mouth rinse 12 h after a single use and 14 days' use. *J Clin Periodontol*, 2005; 32: 335-40.
26. Sharma N, Charles CH, Lynch MC, Qaqish J, McGuire JA, Galustians JG; Adjunctive benefit of an essential oil-containing mouthrinse in reducing plaque and gingivitis in patients who brush and floss regularly: a six-month study. *J Am Dent Assoc*, 2004; 135: 496-504.
27. Lobene RR, Lobene S, Soparker PM; The effect of cetylpyridinium chloride mouthrinse on plaque and gingivitis. *J Dent Res.*, 1977; 56: 595.
28. Ciancio SG; Chemotherapeutic agents and periodontal therapy. Their impact on clinical practice. *J Periodontol*, 1986; 57: 108-11.
29. Holbeche JD, Ruljancich MK, Reade PA; clinical trial of cetylpyridinium chloride mouthwash. *Australian Dent J.*, 1975; 20: 397-404.

30. Roberts WR, Addy M; Comparison of the in vivo and in vitro antibacterial properties of antiseptic mouthrinses containing chlorhexidine, alexidine, cetylpyridinium chloride and hexidine. *J Clin Periodontol*, 1981; 8: 295-310.
31. Kjaerheim V, Skaare A, Barkvoll P, Rølla G; Antiplaque-, antibacterial- and anti-inflammatory properties of triclosan mouthrinses in combination with zinc citrate or polyvinylmethylether maleic acid (PVA-MA) copolymer. *Europ J Oral Sci.*, 1996; 104: 529-34.
32. Waaler SM, Rølla G, Skjörland KK, Ögaard B; Effects of oral rinsing with triclosan and sodium lauryl sulfate on dental plaque formation: a pilot study. *Scand J Dent Res.*, 1994; 101: 192-5.
33. Skaare AB, Herlofson BB, Barkvoll P; Mouthrinses containing triclosan reduce the incidence of recurrent aphthous ulcers (RAU). *J Clin Periodontol*; 1996; 23: 778-81.
34. Gaffar A, Scherl D, Affitto J, Colman EJ; The effect of triclosan on the mediators of gingival inflammation. *J Clin Periodontol*, 1995; 22: 480-4.
35. Hasturk H, Nunn M, Warbington M, Van Dyke TE; Efficacy of a fluoridated hydrogen peroxide-based mouthrinse for the treatment of gingivitis: a randomized clinical trial. *J Periodontol*, 2004; 75: 57-65.
36. Wade AB, Blake GC, Mirza KB; Effectiveness of metronidazole in treating the acute phase of ulcerative gingivitis. *Dent Practit.*, 1966; 16: 440-3.
37. Adamietz IA, Rahn R, Böttcher HD, Schafer V, Reimer K, Fleischer W; Prophylaxis with povidone-iodine against induction of oral mucositis by radiochemotherapy. *Support Care Cancer*, 1998; 6: 373-7.
38. Tenovuo J; Clinical applications of antimicrobial host proteins lactoperoxidase, lysozyme and lactoferrin in xerostomia: efficacy and safety. *Oral Dis.*, 2002; 8: 23-9.
39. Marinho VCC, Higgins JPT, Logan S, Sheiham A; Fluoride mouthrinses for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews*, 2003; 3: DOI: 10.1002/14651858. CD002284.
40. McCullough MJ, Farah CS; The role of alcohol in oral carcinogenesis with particular reference to alcohol containing mouthwashes. *Aust Dent J*, 2008; 53: 302-5.
41. Cole P, Rodu B, Mathisen A; Alcohol-containing mouthwash and oropharyngeal cancer: a review of the epidemiology. *J Am Dent Assoc*, 2003; 134: 1079-87.
42. Lachenmeier DW, Gumbel-Mako S, Sohnius EM, Keck-Wilhelm A, Kratz E, Mildau G; Salivary acetaldehyde increase due to alcoholcontaining mouthwash use: a risk factor for oral cancer. *Int J Cancer*, 2009; 125: 730-5.
43. Hornfedt CS; A report of acute ethanol poisoning in a child: mouthwash verses cologne perfume and after shave. *J Toxicol Clin Toxicol*, 1992; 30: 115-21.
44. Sperry K, Pfalzgraf R; Fatal ethanol intoxication from a household product not intended for ingestion. *J Forensic Sci.*, 1990; 35: 1138-42.
45. Modell JG, Taylor J, Lee JY; Breath alcohol values following the use of a mouthwash. *J Am Med Assoc*, 1993; 270: 2955-6.
46. Penugonda B, Settembrini L, Scherer W, Wittelman E, Strassler H; Alcoholcontaining mouthwashes: effect on composite hardness. *J Clin Dent.*, 1994; 5: 60-2.
47. Settembrini L, Penugonda B, Scherer W, Strassler H, Wittelman E; Alcohol-containing mouthwashes: effect on composite color. *Operative Dent.*, 1995; 20: 14-7.
48. Bellm LA, Epstein JB, Rose-Ped A, Martin P, Fuchs HJ; Patient reports of complications of bone marrow transplantation. *Support Care Cancer* 2000; 8: 33-9.
49. Epstein JB, Epstein JD, Epstein MS, Oien H, Truelove EL; Doxepin rinse for management of mucositis pain in patients with cancer: one week follow-up of topical therapy. *Spec Care Dentist*, 2008; 28: 73-7.
50. Scarpace SL, Brodzik FA, Mehdi S, Belgam R; Treatment of head and neck cancers: issues for clinical pharmacists. *Pharmacotherapy*, 2009; 29: 578-92.
51. Scully C, Sonis S, Diz PD, Oral mucositis. *Oral Dis*, 2006; 12: 229-41.
52. Scully C, Greenman J; Halitosis (breath odor). *Periodontol* , 2008; 48: 66-75.
53. van den Broek AM, Feenstra L, de Baat C; A review of the current literature on management of halitosis. *Oral Dis.*, 2008; 14: 30-9.
54. Dirix P, Nuyts S, Van den Bogaert W; Radiation-induced xerostomia in patients with head and neck cancer: a literature review. *Cancer*, 2006; 107: 2525-34.
55. Eveson JW; Xerostomia. *Periodontol*, 2008; 48: 85-91.
56. Brown LJ, Brunelle, J. A., Kingman, A. Periodontal status in the United States, 1988–1991: prevalence, extent, and demographic variation. *J Dent Res*. 1996; 75 Spec No: 672-83.
57. Oliver RC, Brown L J, Loe H; Periodontal diseases in the United States population. *J Periodontol*, 1998; 69: 269-78.
58. Santos A; Evidence-based control of plaque and gingivitis. *J Clin Periodontol*, 2003; 30 Suppl 5: 13-6.