International Journal of Dentistry and Oral Science (IJDOS)
ISSN: 2377-8075

Analysis Of Dispensing Equipments For Topical Gel Formulations For Management Of Oral Potentially Malignant Disorders

Research Article

Dhanvanth M[1*], Uma Maheshwari TN[2], S Rajeshkumar[3]

[1] Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.
[2] Head of Admin, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.
[3] Associate Professor, Nano-biomedicine Lab, Department of Pharmacology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

Abstract

Aim: The aim of the study is to assess different dispensing equipments for topical gel formulations for management of oral potentially malignant disorders.
Materials and Methods: Different types of dispensers such as glass bottle, plastic container and plastic tube are used. In each dispenser the prepared in-situ gel containing tulsi, turmeric and aloe vera is inserted. After 21 days of shelf life, the three dispensers are monitored. The antioxidant activity is checked separately for each dispenser and evaluated.
Results: On assessing antioxidant activity on three different types of dispenser such as Glass vial, Plastic container and Plastic tube, the most efficient and lowest absorbent dispenser was plastic tube. In 10 µl, the plastic tube showed 0.07 absorbance.
Conclusion: Based on the assessment of antioxidant activity of three different dispensers, the plastic tube showed very good antioxidant activity. Henceforth, the ideology is that better dispenser, the mode of dispensing in-situ gel works better. In future, the plastic tube can be used as a first mode of dispenser in prescribing in-situ gels on oral potentially malignant disorder patients and also for other research studies including topical applications due to its good antioxidant activity.

Keywords: Topical Gel; Dispensing; Glass Bottle; Plastic Tube; Plastic Container; Oral Potentially Malignant Disorders.

Introduction

The mode of dispensing equipments plays an important role in using medications. Different types of dispensing equipments are used such as glass vials, plastic containers and plastic tubes. Glass vials are easy to sterilize with heat. [1] They are transparent and contents inside can be seen. Type IV glass containers are used for oral purposes. The disadvantages of glass bottles are expensive to manufacture. [2] They are fragile and relatively heavy. During heat sterilization, different types of glass containers have the tendency of shedding some portion of the silica into the formulation. The organic materials with plastic containers whose molecules have high molar masses and are formulated of a vast number of repeating comparatively small units termed to as monomers. The monomers will undergo a process known as polymerization, after this a plastic or a sequentially joined chain of polymer is processed. Plastic containers are not breakable. The disadvantages of plastic containers are low physical stability during adsorption, and absorption lightness and interactions between the container and formulations. They have low heat resistant and poor ductility. [3] The plastic containers are not as fragile and transparent as glass, and, therefore, inspection of the substances is impeded. The weight is very light and resistant to leakage. The manufacturing is cheap when compared to glass bottles. [4] They can be easily moulded or remoulded. They have excellent finishing. Plastic containers are chemically bonded and resists to corrosion. They are collapsible. They are impermeable to water. The plastic tubes can be squeezable or collapsible tube which can be used for packing viscous liquids such as in-situ gels. Plastic tubes can be highly effective and special additive such as soft touch that will allow the tube more appealing during use. [5] Plastic tubes are produced by extrusion.It is used as very high standard and also to tight tol-

***Corresponding Author**:
Dhanvanth M,
Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.
E-mail: dhan867@gmail.com

Received: June 11, 2021
Accepted: August 5, 2021
Published: August 14, 2021

Citation: Dhanvanth M, Uma Maheshwari TN, S Rajeshkumar. Analysis Of Dispensing Equipments For Topical Gel Formulations For Management Of Oral Potentially Malignant Disorders. *Int J Dentistry Oral Sci.* 2021;8(8):3698-3701. doi: http://dx.doi.org/10.19070/2377-8075-21000758

erances, compatible with automated processes after extrusion. Topical dosage forms can begels, creams, aerosols, emulsions, pastes, ointments, powders, solutions, and suspensions. The dosage forms are generally allowed for local (not systemic) effect and applied to the skin or oral mucosal surfaces.Some topical drug products are sterile and should be subject to microbial limits. [6, 7] The bottle or jars which are rigid are usually made of glass or polypropylene with a cap screw. The cap liners and inner seals are usually used with solid oral dosage forms. Collapsible tubes are constructed usually from metal and metal lined from LDPE or from a laminated material. The topical delivery systems are self - contained, discrete dosage forms that are designed to deliver drug via intact oral cavity,skin or body surface, namely transdermal, ocular, and intrauterine. [8] Each of these systems is generally marketed in a singleunit soft blister pack or a preformed tray with a preformed cover or overwrap.[9, 10] The compatibility and protection for topical delivery systems are labeled in the same pattern as for topical drug products is concerned. Quality and performance control should be named for the rate controlling membrane.[11] The appropriate limit of microbes should be produced and justified for all delivery system. The containers should allow protection adequately against contamination and detoriation of the intermediate that would cause during transportation andstorage recommendation. The containers should be kept clean and sanitized to assess that they are suitable for their intended use.[12] These containers reactive ability should be controlled, addictive and absorptive so that the quality of the intermediate forms with the specifications. When the containers are reused, they should be cleaned effectively with documented protocols and all previous labels should be removed.[13] The plant Ocimum sanctum, better known as Tulsi or Holy Basil and belongs to the family Lamiaceae. It can also dry tissue secretions and penetrates into deep tissues and has anthelmintic properties. There are also a number of medicinal properties of tulsi including antioxidant, anti-inflammatory, chemo-preventive, anti-carcinogenic, immunomodulatory, etc. have been studied and described in previous studies.[14] In Aloe Vera the aloe term originated from the Arabian word "alloeh" which means shiny and bitter, vera from the latin language which means true or genuine commonly known as a first aid plant because of its rejuvenating, healing or soothing properties. Aloe Vera contains minerlas, vitamins, amino acids, salicylic acids and enzymes. Aloe vera helps in wound healing, and also contains anti-inflammatory, immune-modulatory, and antioxidant properties. Turmeric also called curcumin is derived from the family of curcuma longa.[15] Curcumin is considered to be safe, nontoxic and effective alternative drugs because of its effects on various systems and its therapeutic properties. The curcumin are curcuminoids, which have anti-inflammatory, antioxidant, anti-microbial, neuroprotective, cardio protective and antitumor actions.[16] Oral potentially malignant disorders have been increased statistically high and also have been risk of progressing to carcinoma, but the risk differs according to a range of patients or lesions that are related to various factors. Oral potentially malignant disorders leads to the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or in future. The aim of the study is to assess different dispensing equipments for topical gel formulations for management of oral potentially malignant disorders.[17, 18]

Materials And Methods

Different types of dispensers such as Glass bottle, Plastic container and plastic tube is used. In each dispenser the prepared in-situ gel containing tulsi, turmeric and aloe vera is inserted. After 21 days of shelf life, the three dispensers are monitored. The Antioxidant activity is checked separately for each dispenser and evaluated. In antioxidant activity, DPPH assay was used to test the antioxidant activity of Tulsi, turmeric and aloe vera in-situ gel. Diverse concentrations (2-10 µg/ml) of tulsi, turmeric and aloe vera in-situ gel was mixed with 1 ml of 0.1 mM DPPH in methanol and 450 µl of 50 mMTrisHCl buffer (pH 7.4) and incubated for 30 minutes and evaluated with photometer. Later, the reduction in the quantity of DPPH free radicals was assessed dependent on the absorbance at 517 nm. BHT was employed as control. The percentage of inhibition was determined from the following equation,

% inhibition= Absorbance of control - Absorbance of test sample × 100/Absorbance of control

Results

On assessing antioxidant activity on three different types of dispenser such as Glass vial, Plastic container and Plastic tube, the most efficient and lowest absorbent dispenser was plastic tube. In 10 µl, the plastic tube showed 0.07 absorbance. In 20 µl, showed 0.11 Absorbance. In 30 µl, showed 0.1 Absorbance. In 40 µl, 0.1 Absorbance and in 50 µl, showed 0.11[Figure 1, 2] Absorbance. These absorbance rates at different concentrations (µl) of plastic tube showed comparatively better absorbance than glass bottle and plastic container. The spectrophotometer showed readings with antioxidant activity assay of in-situ gel in glass bottle, plastic container and plastic tube. The spectrophotometry readings of antioxidant assay shows that 20 µL of plastic tube have more absorption percentage of about 0.1%.

Figure 1. Types of dispensing equipments with in-situ gel.

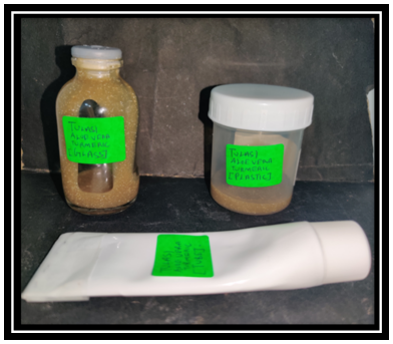


Figure 2. Anti-oxidant activity on in-situ gel on glass bottle, plastic container and plastic tube.

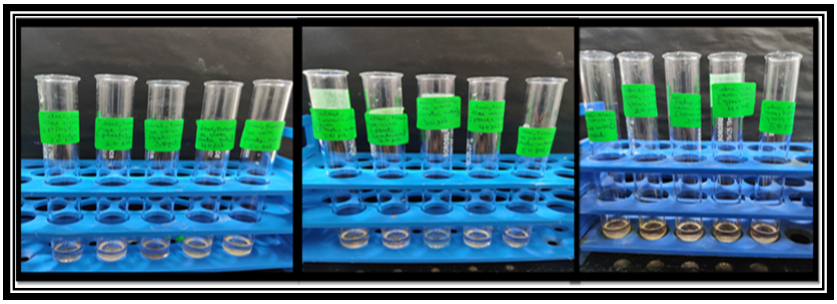
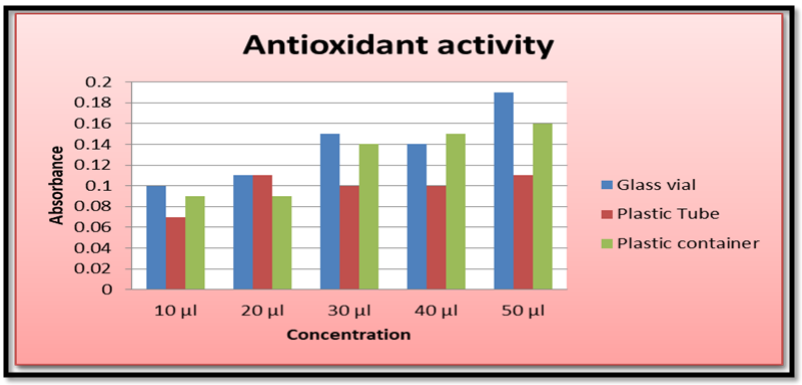


Figure 3. Anti-oxidant activity testing using in-situ gel containing tulsi, aloe vera and turmeric on glass bottle, plastic container and plastic tube in 10 µL, 20 µL, 30 µL, 40 µL and 50 µL in test tube containing 1ml of DPPH.



Discussion

Oral potentially malignant disorders (OPMDs) include a variety of lesions and conditions characterized by an increased risk for malignant transformation to oral squamous cell carcinoma. Leukoplakia and erythroplakia are the most common OPMDs, while special emphasis has been placed on the premalignant nature of oral lichen planus. [19] The selection of dispensing equipment is drug specific and one type of drug cannot be suitable for dispensing all equipment. The choice of dispensing equipment depends upon the number of factors including product stability during processing and storage conditions, type of dosage form, route of administration, chemical nature of the drug. [20] However, glass and plastic containers/tubes are used for the dispensing equipment of topical aerosols on oral liquid formulations. Glass containers are among the primary dispensing equipment that has found use in the pharmaceutical drug dispensing. A large number of pharmaceutical formulations have been packaged using glass containers and dispensed. Glass is an inorganic material mostly silicates or mixture of materials which when heated up and then cooled, solidifies without crystallization.[21] Glass containers are classified into Type I glass, Type II glass, Type III glass and Type IV glass based on their degree of chemical/hydrolytic resistance to water attack. The glass containers have factors of limited alkalinity and hydrolytic resistance. Glass containers have thermal expansion properties (freeze-drying).[22] The sensitivity of the glass container consist barium or calcium ions. Plastic containers consist of organic materials whose molecules have high molar masses and are composed of a large number of repeating relatively small units referred to as monomers. When these monomers undergo a process known as polymerization, a plastic or a sequentially joined long chain of polymer is formed.[23] This process of polymerization may involve various chemicals which assist the process, such as accelerators, initiators, solvents and catalysts, and as a result, are present in small degree in the plastic formed. These, if found in the plastic after polymerization are generally referred to as process residues. Plastics may also incorporate processing aids e.g., styrene, acrylics, calcium carbonates, lubricants, silicone oil etc., which are usually added to assist a process and additives (e.g., plasticizers, coloring matter, fillers/extenders, light stabilizers, reinforcement etc.,) which modify the plastic chemically or physically in some way. Most plastics derive their names from the type of polymers used during manufacture.[24, 25] Virtually any desired property or characteristics can be achieved during plastic formation by proper manipulation of the properties of the polymers and additives used. Plastic packaging system can broadly be divided into two categories: thermoplastics (thermo softening plastics) and thermosets (thermosetting plastics). Thermoplastics are heat softening materials which are usually rigid at operating temperatures but can be remelted and remoulded when exposed to high temperature and pressure.[26] Thermosets get distinctly infusible or insoluble when exposed to high temperature/ heat, and thus cannot be remelted and remoulded after their initial heat forming Gels are semisolid preparations that contain small inorganic particles or large organic molecules interpenetrated by a liquid. Gels made of inorganic materials are usually two - phase systems where small discrete particles are dispersed throughout the dispersion medium. When the particle size of the dispersed phase is larger, they are referred to as magmas. Gels made of organic molecules are single - phase systems, where no apparent physical boundary is seen between the dispersed phase and the dispersion medium. In most cases, the dispersion medium is aqueous.[27] Hydro alcoholic or oleaginous dispersion media are also used in some cases. Unlike dispersed systems like suspensions and emulsions, movement of the dispersed phase is restricted in gels because of the solvated organic macromolecules or interconnecting three - dimensional networks of particles. Gels are attractive delivery systems as they are simple to manufacture and suitable for

administering drugs through skin, oral, buccal, ophthalmic, nasal, otic, and vaginal routes.[28] They also provide intimate contact between the drug and the site of action or absorption.In situ gels are the hydrogel systems that are applied as liquids (solutions or suspensions) at room temperature but undergo sol-to-gel transformation, also called gelation, due to change in specific physicochemical parameters like pH, temperature and ionic strength in the environment. Primary packaging and dispensing systems that are able to handle non-preserved drug products need to prevent bacterial ingress into the drug product. These dispensing systems build a physical barrier to microbes at the interface to the outside. Sealing needs to be sufficiently strong to break product microfilms. Modern systems make use of elastomer elements or spring-loaded tips sealing the dispensing orifice. They can effectively protect non-preserved formulations or allow for lower concentrations.[29, 30-37]

Conclusion

Based on the assessment of antioxidant activity of three different dispensers, the plastic tube showed very good antioxidant activity. Henceforth, the ideology is that better dispenser, the mode of dispensing in-situ gel works better. In future, the plastic tube can be used as a first mode of dispenser in prescribing in-situ gels on oral potentially malignant disorder patients and also for other research studies including topical applications due to its good antioxidant activity. Depending on the needs, the content will be protected from environmental influences, such as oxygen, light, or drying and clogging. New systems are able to block microbial contamination and will help reduce or even avoid the need for potentially harmful preservatives. Ideally, innovative dispensing systems support long-term treatment schedules through attractiveness, convenience, intuitive design, and match with the daily activity of the patients.

References

[1]. Nasa P. A Review on Pharmaceutical Packaging Material. World Journal of Pharmaceutical Research, 2014;3(5): 344-368.
[2]. Pillai SA, Chobisa D, Urimi D, Ravindra N. Pharmaceutical glass interactions: a review of possibilities. Journal of Pharmaceutical Sciences and Research. 2016 Feb 1;8(2):103.
[3]. Shivsharan US, Raut ES, Shaikh ZM. Packaging of cosmetics: A review. Journal of pharmaceutical and scientific innovation. 2014;3(4):286-93.
[4]. Advani, S.G. and Sozer, E. M. Process Modeling in Composites Manufacturing (2nd Ed.). Taylor and Francis Group, LLC.2010.
[5]. Dean DA, Evans ER, Hall IH, editors. Pharmaceutical packaging technology. CRC Press; 2005 Jul 12.
[6]. Pareek VI, Khunteta A. Pharmaceutical packaging: current trends and future. Int J Pharm Pharm Sci. 2014;6(6):480-5.
[7]. Annex WH. 9: Guidelines on packaging for pharmaceutical products. WHO Technical Report Series. 2002.
[8]. Yam, K. L., "Encyclopedia of Packaging Technology", John Wiley & Sons, 2009.
[9]. Soroka, W, "Fundamentals of Packaging Technology", 2002.
[10]. Silva GA. Neuroscience nanotechnology: progress, opportunities and challenges. Nat Rev Neurosci. 2006 Jan;7(1):65-74. PubmedPMID: 16371951.
[11]. Wang ZL. Characterization of nanophase materials Wiley.
[12]. Vasir JK, Reddy MK, Labhasetwar VD. Nanosystems in drug targeting: opportunities and challenges. Current Nanoscience. 2005 Jan 1;1(1):47-64.
[13]. Lane , N. F,inBhushan , B. , Ed., Springer Handbook of Nanotechnology ,Springer - Verlag , Berlin; 2004.
[14]. Goodsell DS. Bionanotechnology: lessons from nature. John Wiley & Sons; 2004 Apr 16.
[15]. Fritz J, Baller MK, Lang HP, Rothuizen H, Vettiger P, Meyer E, et al. Translating biomolecular recognition into nanomechanics. Science. 2000 Apr 14;288(5464):316-8. PubmedPMID: 10764640.
[16]. Xu XH, Chen J, Jeffers RB, Kyriacou S. Direct measurement of sizes and dynamics of single living membrane transporters using nanooptics. Nano Letters. 2002 Mar 13;2(3):175-82.
[17]. Li J, Papadopoulos C, Xu J. Growing Y-junction carbon nanotubes. Nature. 1999 Nov;402(6759):253-4.
[18]. Ajazuddin, Alexander A, Khan J, Giri TK, Tripathi DK, Saraf S, et al. Advancement in stimuli triggered in situ gelling delivery for local and systemic route. Expert Opin Drug Deliv. 2012 Dec;9(12):1573-92. PubmedPMID: 23075325.
[19]. Ruel-Gariépy E, Leroux JC. In situ-forming hydrogels--review of temperature-sensitive systems. Eur J Pharm Biopharm. 2004 Sep;58(2):409-26. PubmedPMID: 15296964.
[20]. Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med. 2007 Nov;36(10):575-80. PubmedPMID: 17944749.
[21]. Warnakulasuriya S, Reibel J, Bouquot J, Dabelsteen E. Oral epithelial dysplasia classification systems: predictive value, utility, weaknesses and scope for improvement. J Oral Pathol Med. 2008 Mar;37(3):127-33. PubmedPMID: 18251935.
[22]. El-Naggar AK, Chan JK, Grandis JR, Takata T, Slootweg PJ. WHO Classification of Head and Neck Tumours 4th Edition. 4th éd.
[23]. Napier SS, Speight PM. Natural history of potentially malignant oral lesions and conditions: an overview of the literature. J Oral Pathol Med. 2008 Jan;37(1):1-10. PubmedPMID: 18154571.
[24]. van der Waal I. Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification and present concepts of management. Oral Oncol. 2009 Apr-May;45(4-5):317-23. PubmedPMID: 18674954.
[25]. Warnakulasuriya S, Ariyawardana A. Malignant transformation of oral leukoplakia: a systematic review of observational studies. J Oral Pathol Med. 2016 Mar;45(3):155-66. PubmedPMID: 26189354.
[26]. Visiongain. Dermatological Drugs: World Market 2009;2011-2026.
[27]. CDER. Center for Drug Evaluation and Research, Novel New Drugs Report. January 2011.
[28]. Carter, SJ. Cooper and Gunn's Dispensing for Pharmaceutical Students, twelthed, CBS publishers 2008:357- 391.
[29]. Dimbleby V. Glass for pharmaceuticl purpose. J. Pharmacy. Pharmcology 2011;5(1): 969-989.
[30]. Ambrosio TJ. Packaging of Pharmaceutical Dosage Form. In: RT Banker SG, Rhodes CT. (Eds) Modern Pharmaceutics, Marcel Dekker Inc. New-York 2002:588-606
[31]. Mohapatra S, Leelavathi L, Rajeshkumar S, Sakthi DS, Jayashri P. Assessment of Cytotoxicity, Anti-Inflammatory and Antioxidant Activity of Zinc Oxide Nanoparticles Synthesized Using Clove and Cinnamon Formulation--An In-Vitro Study. Journal of Evolution of Medical and Dental Sciences. 2020 Jun 22;9(25):1859-65.
[32]. Aathira CM, Arivarasu L, Rajeshkumar S. Antioxidant and Anti-Inflammatory Potential of Chromium Picolinate Mediated Zinc Oxide Nanoparticle. Journal of Pharmaceutical Research International. 2020 Aug 26:118-21.
[33]. Sharma Mn, Rajasekar A, Rajeshkumar S. Antioxidant Activity Of Grape Seed Mediated Tio2 Nanoparticles: An In Vitro Study. Plant Cell Biotechnology And Molecular Biology. 2020 Aug 26:24-31.
[34]. Ponnanikajamideen M, Rajeshkumar S, Vanaja M, Annadurai G. In Vivo Type 2 Diabetes and Wound-Healing Effects of Antioxidant Gold Nanoparticles Synthesized Using the Insulin Plant Chamaecostuscuspidatus in Albino Rats. Can J Diabetes. 2019 Mar;43(2):82-89.e6. PubmedPMID: 30413371.
[35]. Ananya R, Roy A, Rajeshkumar S, Lakshmi T. Antioxidant And Cytotoxic Effects Of Silver Nanoparticles Synthesised Using Hing Oil. Plant Cell Biotechnology And Molecular Biology. 2020 Aug 24:1-8.
[36]. Preeja Rp, Arivarasu L, Rajeshkumar S. Antimicrobial And Antioxidant Activity Of Phyllanthusniruri Mediated Silver Nanoparticles. Plant Cell Biotechnology And Molecular Biology. 2020 Aug 25:30-7.
[37]. Anjum AS, Anitha R, Rajeshkumar S. Thangavelu Lakshmi Synthesis of White Pepper Oleoresin Mediated Silver Nanoparticles and its Antioxidant Effect. Biomedicine. 2019;31(1):165-9.