ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Spray Pattern of Oral Cavity Sprays Containing the Herbal Extracts

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ABSTRACT

The dispersion of oral spray from the spray nozzle into the oral cavity should be considered for its spray pattern which can influence the acceptance of the user. The developed oral cavity sprays containing chili extract and other volatile oils were tested for their spray patterns. To determine the spray dispersion into the oral cavity this study employed the high speed camera to take and capture the photo when they sprayed into the air. The six oral spray products comprising herbal extracts were tested for their spray pattern with the high speed camera which their spray angle was measured to indicate and compare the spray behavior. The speed for taking the photo was 1/3000 sec and photo was selected at the order of 120 which the detection of spray angle was performed at the position close to the spray nozzle. The antimicrobial activities of the oral cavity sprays against *Staphylococcus aureus* and *Candida albican* were determined with agar diffusion method. The doxycycline 2 µg/ml and clotrimazole 40 µg/ml solutions were used as positive control for antibacterial and antifugal activities, respectively. The spray angle of six oral cavity sprays (code O1, O2, O3, O4, O5 and O6) were 48.5, 41.0, 32.1, 24.9, 47.0, 31.0° with the spraying time of 0.151333, 0.154333, 0.144667, 0.148667, 0.192000, 0.061667 sec, respectively. This obtained spray pattern data could be used to adjust the spray component such as the amount of viscosity inducing agent for developing the oral cavity spray with proper spraying characteristic. The developed oral sprays containing chili extract and volatile oils could inhibit *Staphylococcus aureus* and *Candida albican* with capsaicin dose denpendence. From the above results the spray angle obtained from the high speed camera could be employed to signify the spray pattern of the oral cavity spray containing the herbal extracts.

Keywords: spray pattern, oral cavity spray, herbal extracts

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ISSN: 0975-8585

INTRODUCTION

The oral cavity spray has been employed as antiseptic or delivery system for other active compounds. Glyceryl trinitrate (NTG) oral spray showed the potent coronary vasodilators in patients with increased coronary vasomotor tone [1]. Isosorbide dinitrate (ISDN) oral spray for lingual and buccal delivery could provide the rapid onset of action than sublingual tablet administration because the drug could be absorbed from the tablet only after its dissolution [2]. Butyl-cyanoacrylate spraying into oral cavity to achieve as a thin and elastic film was a sufficient hemostatic treatment [3]. The evaluation for the effectiveness of oral spray has been performed with many techniques. The viscosity or antimicrobial activities tests have been mostly investigated. From histomorphologic analysis of the lung, liver, stomach, and kidney, it revealed that when the throat of the animal was protected, an oral spray of isobutyl cyanoacrylate which was the adhesive did not result in any aspiration of the material or any discernible changes in the respiratory and gastrointestinal systems or in the vital organs [4]. The tracking of radiolabelled drug molecule has been employed to observe the drug distribution such as in nasal cavity. Visual spread pattern of 99mTc-diethylenetriaminepenta acetic acid (DTPA) radiolabelled ketorolac tromethamine formulation following nasal administration was tested in healthy subjects. The majority of the radiolabelled intranasal dose was deposited in the nasal cavity. The fraction of the dose recorded from the lung regions averaged <0.5%, and was considered to represent scattered radiation rather than true pulmonary deposition. The visual spread pattern within the nasal cavity was most uniform following administration in the upright position regardless of inhalation manoeuvre [5]. Effect of the metered-dose inhaler (MDI) spray angle was studied for the aerosol penetration efficiency through a human oral airway using the computer simulation of the fluid flow and the aerosol transport patterns within a three-dimensional human airway model. The aerosol entrance angle has a strong effect on the MDI penetration efficiency, particularly at the higher flow rate [6]. The application of high speed camera is interesting to use to evaluate the spray pattern such as spray angle of oral spray.

The aim of this study is to observe the spray pattern of developed oral cavity sprays during their spraying and to test their antimicrobial activity.

MATERIALS AND METHODS

Materials

Capsicum tincture (0.05% capsaicin in chili extract) code 81270 control No. R 18506, Bangkok Lab & Cosmetic Ltd., Ratchaburi, Thailand was used as received. Tween 80, dimethyl sulfoxide (DMSO), peppermint oil, cinnamon oil, clove oil and other chemicals were purchased from PC Drug Co., Ltd., Bangkok, Thailand. Tryptic Soy Agar (TSA) (lot No. 3056695, Difco, USA.), Tryptic Soy Broth (TSB) (lot 4259, Difco, USA.), Sabouraud Dextrose Agar (SDA) (lot 6166081, Difco-TM, Becton Dickinson and Company, USA) and Sabouraud Dextrose Broth (SDB) (lot 6345690, Difco-TM, Becton Dickinson and Company, USA) were used as received. Clotrimazole and doxycycline hyclate were kindly supported from T Man Pharma Co. Ltd., Bangkok, Thailand.

ISSN: 0975-8585

Methods

Spray pattern

The developed oral cavity sprays containing 0.005%, 0.003% and 0.001% w/w capsaicin (code No. O1, O2 and O3) were prepared using the capsicum tincture and combined with the volatile oils. The three commercial products were also used as received as code No. (O4, O5 and O6). To determine the spray dispersion into the oral cavity this study employed the high speed camera (Photron, FASTCAM-APX RS, Fujimi 1-1-8, Chiyoda-ku, Japan) to take the photo when the oral cavity sprays were sprayed through the spray nozzle into the air. The six oral spray products comprising herbal extracts were tested for their spraying pattern with the high speed camera which their spray angle was measured to indicate and compare the spray behavior. The speed for taking the photo was 1/3000 sec and photo was selected at the order of 120 which the detection of spray angle was performed at the position close to the spray nozzle. The spray characteristic by visual observation was also recorded.

Antimicrobial test

For the antimicrobial activity test the developed oral cavity sprays (O1, O2 and O3) were tested using the cup agar diffusion technique. The 10% DMSO containing 0.5%v/v tween 80 was used as the control solvent. Once an actively growing broth culture or suspension of microbes was obtained then the bacteria was inoculated and prepared by adjusting the turbidity of an actively growing broth culture in used broth to an optical density at 530 nm equivalent to $1x10^8$ cfu/ml. A sterile swab was dipped into the adjusted suspension before rotating and pressing on the inside wall of the tube. The inoculated microbe was spread on TSA for bacteria (*Staphylococcus aureus*) and SDA for fungi *(Candida albicans*) in three directions to ensure the complete spreading of the agar surface. Plates were opened for a few minutes to dry the spread culture. The sterile cyclinder cup was filled with the tested sample of 150 µL/cup and placed for 30 min before incubated at 37 °C for 48 hrs. The antimicrobial activity was measured as the diameter (cm) of the clear zone of growth inhibition. The tests were carried out in triplicate and the mean clear zone ± S.D. was calculated. The sterile cyclinder cup filled with 10% DMSO containing 0.5%v/v tween 80 at the same amount of those test samples were employed as the negative control. The doxycycline 2µg/ml and clotrimazole 40 µg/ml solutions were used as positive control for antibacterial and antifugal activities, respectively.

RESULTS AND DISCUSSION

Spray pattern

The high speed camera could effectively take and capture the photo of droplets dispersing in the environmental space. The obtained data are shown in Table 1 and Fig. 1. The spray angle of O1 was widest whereas that of O4 was smallest. The spray angle of O1 was wider than that of O2 and O3, respectively. The higher amount of capsaicin indicating the higher amount of capsicum tincture in the formula could decrease the solubility of some substances thereafter the viscosity of the spray solution decreased and the spray angle was

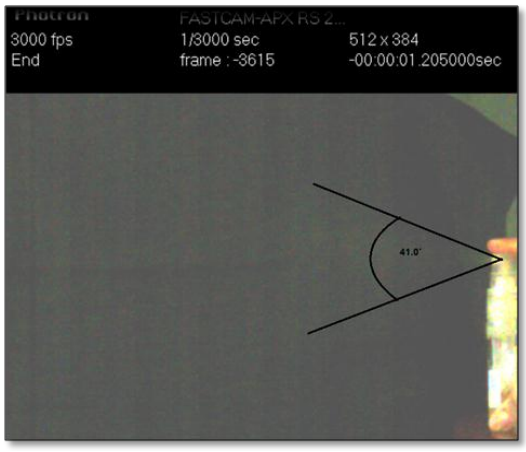
ISSN: 0975-8585

wider. Typically, the spray angle is decreased as the viscosity and surface tension are increased whereas it is increased as the temperature of the solution is increased [7]. This result could be used to adjust the spray component such as the amount of viscosity inducing agent for developing the oral cavity spray with proper spraying characteristic. The longest time interval of spraying was found for O5 whereas that of O6 was shortest. The shorter and longer time for each spraying indicated the ease and difficulty, respectively, of pressing the spray nozzle. The commercial O5 showed the longest this value.

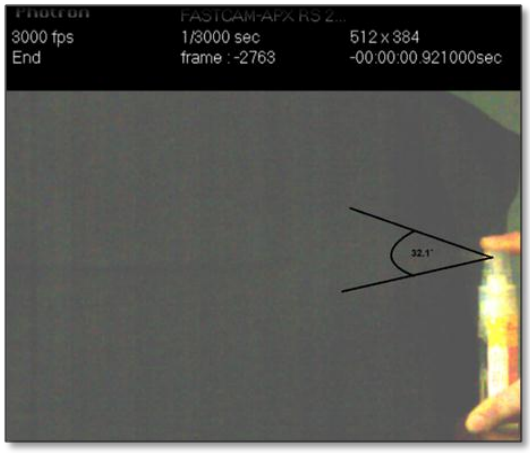
Table 1 Spray angle, time and appearance of different oral sprays.

Formula code	Spray angle (°)	Time for each spray (sec)	Spray appearance
O1	48.5	0.151333	Fine droplets
O2	41.0	0.154333	Fine droplets
O3	32.1	0.144667	Fine droplets
O4	24.9	0.148667	Line
O5	47.0	0.192000	Very fine droplets
O6	31.0	0.061667	Fine and small droplet

O1



O2



ISSN: 0975-8585

Fig. 1 Spray pattern exhibiting the spray angle of different oral sprays obtained from high speed camera.

Antimicrobial activity

The developed oral cavity sprays could inhibit *S. aureus* and *C. albicans* with the capsaicin dose dependence as shown in Table 2. Some researchers reported the antimicrobial activity of capsaicin against *Listeria monocytogenenes, Staphylococcus aureus, Salmonella typhimurium, Helicobacter pylori* and *Bacillus cereus* (8,9). The solvent showed the small antimicrobial activity against *S. aureus* whereas there was no inhibition zone for *C. albicans*. These results indicated that these developed oral cavity sprays could inhibit the microbial growth. The difference in degree of hot or spicy taste owing to the various amount of capsaicin will be useful for the users to select the best one that is suitable for themselves. The awakeness obtained from the taste of these developed solutions will also be the advantage of these developed systems.

Table 2 Antimicrobial activity of oral cavity sprays

Microorganisms / Test samples	Clear zone (cm)	
	Staphylococcus aureus	*Candida albicans*
O1	1.70 ± 0.05	2.35 ± 0.15
O2	1.55 ± 0.05	2.00 ± 0.01
O3	1.40 ± 0.01	1.75 ± 0.05
Solvent	0.78 ± 0.02	(-)
Doxycycline 2µg/ml	2.15 ± 0.05	N/A
Clotrimazole 40 µg/ml	N/A	2.55 ± 0.05

(-) = no clear zone; N/A=not determined

ISSN: 0975-8585

CONCLUSION

The high speed camera could be useful to use for evaluating the spray pattern of oral cavity sprays containing the capsicum extract and volatile oil. These developed oral cavity sprays exhibited the antimicrobial activities against *S. aureus* and *C. albicans*.

ACKNOWLEDGEMENTS

This research work was kindly supported by Government-Industries Cooperation Project, Division of Research & Evaluation, Commission on Higher Education, Ministry of Education, Thailand (Year 2010; Project: Oral Cavity Spray Containing Chili Extract and Essential Oils). We would like to thank Bangkok Lab & Cosmetic Ltd., Ratchaburi, Thailand for his kind support the capsicum tincture. I would like to express my appreciation to Faculty of Pharmacy, Silpakorn University for the facility and support.

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